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COMMITTEE PRINT

DIETARY GOALS FOR THE
UNITED STATES—SUPPLEMENTAL VIEWS

PREPARED BY THE STAFF OF THE
SELECT COMMITTEE ON NUTRITION
AND HUMAN NEEDS
UNITED STATES SENATE



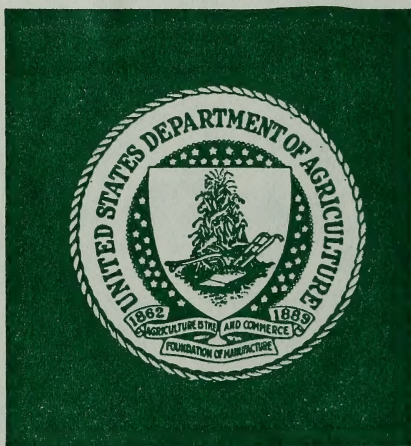
NOVEMBER 1977

Printed for the use of the Select Committee on Nutrition
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U.S. DEPT. OF AGRICULTURE
NATIONAL AGRICULTURE

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¹ Statement of the National Cattlemen's Association is printed in the hearing "Diet Related to Killer Diseases, III," March 24, 1977; statement of the United Egg Producers is printed in the hearing "Diet Related to Killer Diseases, VI," July 26, 1977. For sale by the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

FOREWORD

In February of this year, the Senate Select Committee on Nutrition and Human Needs, released a report entitled "Dietary Goals for the United States."

In developing the report's recommendations, the Select Committee evaluated a wide variety of scientific data and testimony. Witnesses testifying before the committee included the Assistant Secretary for Health—the Nation's top health official; representatives from the National Institutes of Health; and other individuals with expertise in the area of diet and preventive medicine. The findings and recommendations of professional panels in the United States and other countries were also considered, including the Report of Inter-Society Commission for Heart Disease Resources which drew upon the work of 28 participating professional organizations. Finally, nutritionists, including Dr. Mark Hegsted, the first president of the National Nutrition Consortium, and health policymakers including Dr. Philip Lee, the first Assistant Secretary for Health, HEW, consulted with the staff during the report's development.

Nonetheless, as the first such statement by any branch of the Federal Government, "Dietary Goals for the United States," has generated a great deal of interest, debate, and controversy among consumers, scientists, and industry representatives.

Two industries—meat and egg producers—requested additional hearings to express their views. These were held on March 24 and July 26 respectively.¹

The National Live Stock and Meat Board sent the committee the names of 24 experts "whose professional backgrounds and experience in recent years suggest intimate knowledge of the fact, fallacies and controversy which surround the concepts or hypotheses of diet as a precursor to atherosclerosis and other of the degenerative diseases in America and elsewhere." Their opinions were sought along with the views of other experts. In all, approximately 50 additional opinions were solicited.

In an effort to present a complete hearing record and basis for further considerations of national dietary guidelines, the committee is printing in this publication all responses in their entirety, as well as important reports and surveys on the subject.

GEORGE MCGOVERN,
Chairman.

CHARLES H. PERCY,
Ranking Minority Member.

¹ All volumes of the committee's hearings "Diet Related to Killer Diseases," are on sale by the Superintendent of Documents, Government Printing Office, Washington, D.C. 20402.

CHAPTER I

Review of Dietary Goals of the United States

THE LANCET,* APRIL 23, 1977

An important document has just been published by the U.S. Senate Select Committee on Nutrition and Human Needs.¹ The chairman, Senator George McGovern, expresses his conviction that "the eating patterns of this century represent as critical a public health concern as any now before us. We must acknowledge and recognize that the public is confused about what to eat to maximize health. . . . We have an obligation to provide practical guides to the individual consumer as well as set national dietary goals. . . . Such an effort is long over-due". The committee sets out six dietary goals, based on scientific testimony and recent reports, including fifteen sets of guidelines, mostly about prevention of coronary heart-disease, from expert and official bodies.

Goal one is to increase carbohydrate consumption to between 55 percent and 60 percent of the energy (caloric) intake. The committee shows its professionalism by starting with what should be increased, to compensate for the reductions entailed by the other five goals. Present total carbohydrate consumption in the U.S.A., as in Britain, is 46 percent of dietary energy, about half in the form of sugar. The increase should be in the form of complex carbohydrates or starchy foods such as vegetables, fruits, and whole grains that also contain many other nutrients including dietary fibre. A day's allowance of protein from whole-grain cereals, legumes, and nuts costs less than the equivalent amount from most types of meat. This first goal will surprise those (one hopes few of them are medical people) who still imagine that starchy foods are unhealthy or that bread and potatoes are especially fattening.

Goal two is to reduce fat consumption from over 40 percent down to 30 percent of energy intake. This goal is in the same direction as official British advice² but goes further. Thirty percent of fat is rather less than was available in Britain during the 1939-1945 war but more than the content in traditional Mediterranean cookery. Fats are the most concentrated source of energy in the diet and so favour obesity. Many fats provide empty calories—they are not associated with the mixture of micronutrients found with complex carbohydrates. They are, in addition, epidemiological associations of breast and colon cancer with fat intake, unsaturated as well as saturated.³

*A British medical journal.

¹ Dietary Goals for the United States. U.S. Senate Committee on Nutrition and Human Needs. Washington, D.C. 1977.

² Diet and Coronary Heart Disease. Report of the advisory panel of the Committee on Medical Aspects of Food Policy (Nutrition). H. M. Stationery Office, 1974.

³ Royal College of Physicians of London and British Cardiac Society. *Jl R. Coll. Physcns Lond.* 1976, 10, 213.

The next two goals concern the nature of the dietary fats. Goal three is that saturated fats should be reduced to 10 percent of total calories and balanced with around 10 percent monounsaturated and 10 percent polyunsaturated fats. For comparison the present British diet⁴ is 21 percent saturated, 16 percent monounsaturated, and 4 percent polyunsaturated fats (total 41 percent of energy intake). The reasons for reducing saturated and increasing polyunsaturated fats are well enough known.⁵⁻⁷ The fourth goal is reduction of dietary cholesterol to about 300 mg a day because it too tends to increase plasma-cholesterol—though seemingly more in some individuals than in others.⁸ One egg contains some 250 mg of cholesterol in the yolk, but servings of liver and kidney can provide more.

The fifth goal is to reduce refined sugar to 15 percent of dietary energy from the present estimated 24 percent in the U.S.A. Refined sugar in Britain contributes about 20 percent of total calories.⁴ While most experts believe that no clear links have been established between sucrose and heart-disease, refined sugars provide empty calories and are associated with dental caries. A major source of refined sugar is soft drinks; in the U.S.A. their consumption has doubled in the past 15 years and the report suggests they should be much reduced or even eliminated from the diet.

The sixth goal is reduction of salt intake to approximately 3 g a day. Present consumption in the U.S.A. is 6–18 g, but the physiological requirement probably averages only 0.5 g a day. Sodium intake is more and more determined by good processors rather than by the individual. This extensive addition of salt to our foods disturbs the natural balance with potassium and may well favour the development of essential hypertension.

Looking at the foods which can be used to achieve these six nutritional goals, the report shows that highly processed foods are the most likely to be high in saturated fat and sugar or salt. In addition they very likely contain unnecessary additives such as colouring. Soft drinks account for more of the artificial colour intake in children than any other type of food or drink. For school and institutional catering, unprocessed foods, cooked on the premises, have sociological and economic as well as nutritional advantages over convenience foods.

Nutrition education of the public is poor. The seven (or four) basic food groups are out of date; they were not designed to meet current nutritional problems. Television is said to be the primary source of information for the American public today, but the advertisements for food and drink are unbalanced towards alcoholic beverages, confectionery, and highly processed foods while fresh fruit, vegetables, fish, and nuts get hardly any time. A similar picture can be seen in Britain.⁹ Food labelling should show not only the essential nutrients but also the percentage and type of fats and of sugar, the amount of cholesterol and of salt, and the caloric content. The new U.S. goals are similar to

⁴ Household Food Consumption and Expenditure, 1974: annual report of the National Food Survey Committee. H.M. Stationery Office, 1976.

⁵ *Lancet*, 1975, ii, 398.

⁶ Miettinen, M., Karvonen, M. J., Turpeinen, O., Elosno, R., Paavilainen, E. *ibid.* 1972, ii, 835.

⁷ O'Brien, J. R., Etherington, M. D., Jamieson, S. *ibid.* 1976, i, 878.

⁸ Mistry, P., Nicoll, A., Niehaus, C., Christie, I., Janus, E., Lewis, B., *Circulation*, 1976, 54, suppl. 11–178.

⁹ Truswell, A. S. *Näringsforskning* (Swedish Nutrition Foundation), 1975, 20, suppl. 13, p. 42.

Scandinavian recommendations on a healthy diet, published in 1968¹⁰ and subsequently incorporated in the Swedish Diet and Exercise programme and in the proposed Norwegian nutrition and food policy.¹¹ The American goals will be welcomed by people who have thought seriously about the diet of modern Western man. Their major blind-spot is to ignore alcohol consumption, which is increasing fast along with its pernicious effects.¹²

¹⁰ Medicinska sunpunkter på folkkosten i de nordiska landerna. *Vår fola*, 1968, 20, 3 (for English translation see Davidson, S., Passmore, R., Brock, J. F., and Truswell, A. S. Human Nutrition and Dietetics, p. 652. Edinburgh, 1975).

¹¹ Royal Norwegian Ministry of Agriculture Report No. 32 to the Storting (1975-76) on Norwegian nutrition and food policy. Oslo.

¹² Glatt, M. M. *Proc. R. Soc. Med.* 1977, 70, 202.



CHAPTER II

A. LETTER FROM SENATOR GEORGE McGOVERN REQUESTING ADDITIONAL MEDICAL OPINIONS ON DIETARY GOALS FOR THE UNITED STATES

U.S. SENATE,
SELECT COMMITTEE ON
NUTRITION AND HUMAN NEEDS,
Washington, D.C., May 1977.

DEAR DR. ————. Please find enclosed a copy of the Senate Select Committee on Nutrition and Human Need's recently issued publication, *Dietary Goals for the United States*.

In developing the report's recommendations, the staff of the Select Committee evaluated a wide variety of scientific data and testimony. Witnesses before the Committee included the Assistant Secretary for Health—the Nation's top health official, representatives from the National Institutes of Health, and many doctors specializing in the area of diet and preventive medicine.

The recommendations of professional panels in the United States and other countries were also considered as Appendix B indicates. Subsequently, Dr. Kaare Norum, of the University of Oslo Medical School, has released a survey of some 200 doctors from 23 countries (published in the *Norwegian Medical Journal* and in the United States by Senator Kennedy), showing that over 90 percent believe our knowledge about diet and heart disease is sufficient to recommend a moderate change in diet for the population in an affluent society.

I believe that our recommendations are cautious, prudent generalizations, that would have less risks associated with them than our current dietary habits.

Nonetheless, I am aware that the medical community is not of one mind on the "state of the art." In an effort to present a complete hearing record and basis for further considerations, I would be pleased within 30 days to accept for publication your thoughts on the recommendations in general, or any in particular. They may be long or short, written expressly for this record or something you have previously published.

I appreciate your effort in helping the Committee gather as much information as possible on this important topic.

Sincerely,

GEORGE McGOVERN, *Chairman.*

THE UNIVERSITY OF CHICAGO
DIVISION OF THE PHYSICAL SCIENCES
DEPARTMENT OF CHEMISTRY

REPORT OF THE
COMMISSIONERS OF THE
UNIVERSITY OF CHICAGO
FOR THE YEAR 1900-1901
PUBLISHED BY THE UNIVERSITY OF CHICAGO PRESS
CHICAGO, ILL. 1901

THE UNIVERSITY OF CHICAGO
DIVISION OF THE PHYSICAL SCIENCES
DEPARTMENT OF CHEMISTRY
CHICAGO, ILL.

B. RESPONSES

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
NATIONAL INSTITUTES OF HEALTH,
Bethesda, Md., June 13, 1977.

Hon. GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs, U.S.
Senate, Washington, D.C.*

DEAR SENATOR MCGOVERN: I am responding to your letter of May 16.

Between 1964 and 1971, when I served as a staff member of the National Heart and Lung Institute, I was heavily involved in research pertaining to diet and heart disease. In 1971 I joined the staff of the National Eye Institute, and since then my research activities have no longer involved nutrition. Any comments that I could make at this time on the report, "Dietary Goals for the U.S.," prepared by the Senate Select Committee on Nutrition and Human Needs, would be based on information that is at least seven years old, and possibly no longer valid. For this reason, I believe that it would be inappropriate for me to comment on the report.

If I can assist the Committee in any way, given the aforementioned limitation, please let me know.

Sincerely,

FRED EDERER,
*Chief, Office of Biometry and Epidemiology,
National Eye Institute.*

UNIVERSITY OF CALIFORNIA, BERKELEY,
Berkeley, Calif., June 1, 1977.

Senator GEORGE MCGOVERN,
*U.S. Senate,
Washington, D.C.*

DEAR SENATOR MCGOVERN: Several weeks ago you were kind enough to write me with regard to comments that I sent to you on the report "Dietary Goals for the United States."

In your letter, you said that I would probably receive a response from Mark Hegsted or Sheldon Margen.

However, neither of them has said anything to me, either in writing or in conversation.

I have revised my comments slightly because of differences in paging between the xeroxed version and the printed version of the report. Enclosed is the revision. I hope you will include it in the record.

With best regards.

THOMAS H. JUKES.

Enclosure.

[Submitted February 19, 1977 : Revised June 1, 1977]

"DIETARY GOALS FOR THE UNITED STATES"—THE MCGOVERN COMMITTEE REPORT

This report was prepared by the staff of the Select Committee on Nutrition and Human Needs, United States Senate. The Report recommends the following "U.S. Dietary Goals:"

1. Increase carbohydrate consumption to account for 55 to 60 percent of the energy (caloric) intake.
2. Reduce overall fat consumption from approximately 40 to 30 percent of energy intake.
3. Reduce saturated fat consumption to account for about 10 percent of total energy intake; and balance that with poly-unsaturated and mono-unsaturated fats, which should account for about 10 percent of energy intake each.
4. Reduce cholesterol consumption to about 300 mg a day.
5. Reduce sugar consumption by about 40 percent to account for about 15 percent of total energy intake.
6. Reduce salt consumption by about 50 to 85 percent to approximately 3 grams a day.

The Report takes a "Big Brother" attitude towards the public. Americans, and indeed practically all other peoples, have regarded selection of food as a matter of freedom of choice. In the U.S.A. this has led to the remarkable growth of convenience foods, prepared foods, processed foods, and packaged foods, which are offered for sale in addition to a large variety of basic products, especially vegetables and fruits. As a result, the American food supply is the best and most varied in history.

The Report says in the first paragraph of the introduction that "complex carbohydrates, fruits, vegetables and grain products . . . now play a minority role. At the same time, fat and sugar consumption have risen to the point where these two dietary elements alone now comprise at least 60 percent of total caloric intake, an increase of 20 percent since early 1900's." Simple sugars are a leading constituent of many fruits. This statement evidently ignores this fact in computing the percentage of caloric intake supplied by sugar. Furthermore, so-called "complex carbohydrates" (presumably the authors mean starch) are hydrolyzed to the simple sugar "glucose" in the intestinal tract.

Paragraph 3 of the Introduction relates the overconsumption of fat, cholesterol, sugar, salt and alcohol to "six of the ten leading causes of death"; heart disease, cancer, cardiovascular disease, diabetes, arteriosclerosis and cirrhosis of the liver. Actually, it is the overconsumption of calories that has been related to adult diabetes, and to other degenerative diseases that are the consequence of obesity.

On page 9, the statement is made "fat and sugar are relatively low in vitamins and minerals." This statement is incorrect. Fats and sugars are free from vitamins and minerals. The five major nutrients are fats, carbohydrates, proteins, vitamins and minerals. The sentence could be turned around just as logically, to state, "vitamins and minerals are relatively low in fats and sugars." The Report quotes a state-

ment that "improved nutrition might cut the nation's health bill by one third." This is a laudable objective, but it is not realistic. Degenerative diseases inevitably accompany old age. Indeed, health care expenditures increase if the lifespan is prolonged. Dr. John Cairns pointed out that if tobacco were banned from the United Kingdom, the increase in the expected lifespan would simultaneously increase the cost of care of old people, which comes under the category of health care expenditures.

On page 10 the following quotation from Canada's Minister of National Health and Welfare appears:

Even such a simple question as whether one should severely limit his consumption of butter and eggs can be a subject of endless scientific debate.

Faced with conflicting scientific opinions of this kind, it would be easy for health educators and promoters to sit on their hands; it certainly makes it easy for those who abuse their health to find a real "scientific" excuse.

But many of Canada's health problems are sufficiently pressing that action has to be taken even if all scientific evidence is not in.

This is the kind of talk that leads to the popularity of fake "cancer cures."

Page 12 lists the "United States Dietary Goals" (see above)—in other words, the Committee's own dietary goals for Americans. The proposal to increase carbohydrate consumption to account for 55 to 60 percent of the caloric intake is accompanied by a goal of reducing sugar consumption by "almost 40 percent." There is no scientific evidence that sugar is not just as adequate a source of calories as any other carbohydrate. Over-consumption of either starch or sugar produces undesirable consequences of obesity. Simply stated, people like sweet things, and apparently the McGovern Committee believes that people should be deprived of what they like. There is a puritanical streak in certain Americans that leads them to become "do-gooders." One way of achieving this end is to give people a "guilt complex" so that they will deprive themselves of some simple pleasure in order to relieve the guilt they experience when they indulge themselves.

In contrast, there is some health and scientific basis for dietary goals two, three and six. The evidence for deleterious effects of high consumption of saturated fats and of salt is continuing to grow. The goal of reducing cholesterol consumption to about 3 milligrams a day is quite debatable because cholesterol is synthesized by the body, and a reduction of dietary intake of cholesterol leads to increase of its biological synthesis.

The section on "Vitamins and Mineral Sources" states (p. 18) "For many people consumption [of foods containing vitamins and minerals] may be reaching a critical level below which it may be difficult to obtain adequate levels of micro-nutrients from the volumes of food consumed." Some of the micronutrients, especially the trace minerals, are so universally present in foods that deficiencies of them in experimental animals can be produced only by placing the animals in glass cages, allowing them to breathe only filtered air, and supplying highly purified diets. Actually, the consumption of foods of marine origin is a good way of supplying micronutrients, but this is not mentioned.

There is no evidence, in obesity, that increasing the consumption of

complex carbohydrates is likely to "ease the problem of weight control." Spaghetti eaters and potato eaters can become obese just as easily as candy eaters. The statement that high water content can bring satisfaction of appetite is extremely dubious.

The section on "Fruits and Vegetables" states (p. 21) "If fruits and vegetables are used directly from the garden, it is likely that their nutrient content will exceed that of their processed counterparts . . ." It is not feasible to do this during the winter, and it is not possible for most of the urban population at any time of the year.

The statement on page 11 that "Canned produce has significant nutritional value but is generally thought to have retained less nutrients than frozen or fresh" is meaningless unless the nutrients are named and defined.

On page 22, there is a recommendation for a shift to the use of fresh produce; this has much to commend it, but it is a middle-class luxury for the inhabitants of the developed countries. Indeed, the authors of the Report seemed reluctant to come to grips with the problems involved in supplying large urban populations with food. Food additives, to which these authors obviously object, are indispensable for this purpose.

On page 25, the authors incorrectly state that "surprisingly few studies" have considered the nutritional difference between whole wheat flour and white flour. Actually, whole wheat contains phytic acid, which interferes with the utilization of calcium and zinc and iron to the extent that zinc deficiency can be produced by a diet high in phytic acid, most of which is removed during the refining of wheat flour. Another problem with whole wheat flour is that it easily becomes rancid. There is a vast literature on this subject, particularly the experiences in World Wars I and II. One of the main lessons of history, repeated during both World Wars, is that human beings prefer white flour to whole wheat flour, in a proportion of about 10 to 1, and after each War, the public has returned on its own to white bread.

On pages 37-42 there are some good points about the undesirable increase of the percent of calories supplied by fat. However, they do not mention the obvious possibility that if sugar consumption had not been maintained at a constant level, but had declined, the consumption of fat would probably have increased even more.

Some good points are made on page 33 regarding the parallel between cancer and the consumption of diets high in fats. This parallel may be a good reason for increasing the intake of carbohydrates, including sugar. The same remarks apply to the discussion of heart disease and high fat diets.

On page 43, the Report states that its Figure 3, a table of sugar use, "shows that various kinds of sugar accounted for only about 32 percent of total carbohydrate consumption in the period 1909 to 1913. However, by 1976, sugar had replaced starch, or complex carbohydrates, as the predominant carbohydrate energy source." This implication of a recent increase in sugar consumption is incorrect. The fact is that sugar consumption has remained constant per capita in the United States for about fifty years, except for the war years. This is revealed in the following figures from Table 9, page 44, of the Report:

REFINED SUGAR, ESTIMATED PER CAPITA CONSUMPTION BY TYPE OF USE, SELECTED PERIODS, 1909-13 TO 1971

[In pounds]

Type of use	1909-13	1925-29	1935-39	1947-49	1957-59	1965	1971 (preliminary)
In processed foods:							
Cereal and bakery products.....	4.5	7.7	9.7	12.9	15.4	15.6	17.6
Confectionery products.....	6.5	8.0	8.2	9.8	9.6	10.4	11.0
Processed fruits and vegetables ²	3.0	4.6	4.4	9.0	9.8	9.5	10.4
Dairy products.....	1.5	2.3	2.4	4.6	4.9	5.3	5.8
Other food products ³3	.7	1.2	1.5	1.7	2.5	2.6
Total food products.....	15.8	23.4	25.9	37.8	41.4	43.3	47.4
Beverages (largely in soft drinks).....	3.5	5.0	5.2	10.6	12.6	16.9	22.8
Total processed food and beverages.....	19.3	28.4	31.1	48.4	54.0	60.2	70.2
Other food uses:							
Eating and drinking places ⁴	4.5	5.7	6.3	7.7	7.3	6.2	5.5
Household use ⁵	52.1	65.0	58.8	37.4	33.1	28.2	24.7
Institutional and other use ⁶5	.9	.9	1.3	1.0	1.4	1.1
Total.....	57.1	71.6	66.0	46.4	41.4	35.8	31.3
Total food use.....	76.4	100.0	97.1	94.8	95.4	96.0	101.5
Nonfood use ⁷3	.4	.4	.4	.7	.6	.9
Total consumption.....	76.7	100.4	97.5	95.2	96.1	96.6	102.4

¹ Prepared by Food Consumption Section, Economic Research Service, U.S. Department of Agriculture.² Canned, bottled, and frozen foods (processed fruit and vegetable products); jams, jellies, and preserves.³ Includes miscellaneous food uses such as meat curing, and syrup blending.⁴ Includes hotels, motels, restaurants, cafeterias, and other eating and drinking establishments.⁵ Household use assumed synonymous with deliveries in consumer-sized packages (less than 50 lb.).⁶ Largely for military use.⁷ Includes use in pharmaceuticals, tobacco, and other seafood use.

Source: "Sugars in Nutrition," Levels of Uses of Sugar in the United States, L. Page, B. Friend, 1974.

This table also shows the dramatic drop in household use of sugar. Simultaneously, its use in processed foods and beverages has increased. The net result was no change in per capita sugar consumption, for "sugar is sugar," whether it is consumed in a soft drink, or in a sugar-coated breakfast cereal, or whether it is taken from the sugar bowl on the meal table and added to a beverage or sprinkled over an unsweetened breakfast cereal.

On page 44, a statement by Dr. Jean Mayer which appeared in the New York Times magazine is quoted as follows: "(Sugar calories) increase requirements for certain vitamins, like thiamine, which are needed (for the body) to metabolize carbohydrates."

This quote gives an erroneous impression. "Sugar calories" do not specifically increase the requirement for thiamine. The connection between carbohydrate, including sugar, and thiamine, arises from the fact that thiamine is involved in the oxidation of pyruvic acid, which is an end product of carbohydrate metabolism. However, a Recommended Daily Allowance of thiamine is sufficient to supply the requirement for a diet containing any percentage of carbohydrates as calories. The implication that any carbohydrate "increases the thiamine requirement" is wrong. Raising the fat content of the diet, however, decreases the thiamine requirement below the normal level required for the metabolism of carbohydrates. One of the great nutritional advances of the past thirty years has been the synthesis of thiamine and its use in enrichment of foods, especially enriched flour and breakfast cereals. The

Report is correct in pointing out, at the top of page 45, "No clear links have been established between sugar and heart disease."

One of the basic luxuries of the less well-to-do population in the U.S. and other countries is the consumption of sweetened soft drinks. The emotional appeal of such drinks became obvious when the FDA announced a ban on saccharin. Soft drinks containing sugar are certainly less harmful than wine and liquor. However, reduction of alcohol consumption, in contrast to reduction of sugar consumption, was not listed as one of the goals of the Committee. Actually, reduction of alcohol should be a primary goal, not only for nutritional reasons, but because of the numerous social problems and the problem of highway deaths in which it is involved. Alcohol also has carcinogenic properties.

On page 47 the statement "Reduction in soft drink consumption also offers the advantage of reducing consumption of non-nutritive additives, colors, flavors, and preservatives," reveals the authors' prejudice against these substances. Toxicants occurring naturally in foods are actually more dangerous than the approved "preservatives" that are used in foods.

Goal six of the Committee, for reducing salt consumption, is justifiable, and the exposition of this on page 48 makes some good points. However, the statement, "It has not been appreciated that the sudden salt load of a handful of salted nuts or potato chips, particularly if taken on an empty stomach, can cause a severe migraine six or twelve hours later," is questionable, and certainly anecdotal.

A recommendation on page 65 calls for "a public education program in nutrition based on the foregoing or similar goals. The initial minimum period for the promotion of these dietary goals should be five years." The Report suggests the following tactics in implementing the educational program:

- (1) health and nutrition education in the classroom and cafeterias of our schools;

- (2) nutrition and health education for school food service workers;

- (3) nutrition education in the federally-funded food assistance programs;

- (4) nutrition education conducted by the Extension Service of the Department of Agriculture; and

- (5) extensive use of television to educate the public in the potential benefits of following certain dietary goals.

The problem with this educational program is that it is based on a Committee Report which is largely anecdotal, and contains many vague impressions and prejudices that need scientific foundation. Much more scrutiny, examination and debate by qualified nutritionists is needed before these goals can be accepted.

Several of the objectives of the McGovern Committee Report are praiseworthy, but its general concept of telling Americans what they should eat through a "massive educational campaign" cannot be supported or commended. One of the basic freedoms of human beings is the freedom to choose what they want to eat. At no stage in human history has it been possible to indulge this freedom to the extent that it is today. A profuse choice of all types of food is available in modern supermarkets and grocery stores. The McGovern Committee proposes to mount a campaign that will persuade consumers to fill their shop-

ping carts mainly with whole wheat bread, spaghetti and potatoes. It is a dreary prospect.

The second glaring error in the report is the proposal to cut sugar consumption by the drastic level of 40 percent. This would be a reduction of about 40 pounds per year. To replace this, it would be necessary, in terms of calories, to eat 202 pounds of potatoes, even if the fat content of the diet were kept constant. The proposed cut in fat calories would require a proportionate increase in carbohydrates, so that actually more sugar rather than less would most likely be consumed. Indeed, it has been pointed out by Stare that, for the past fifty years, "sucrose has made up about one third of the carbohydrate calories, with starch providing about two thirds."

VETERANS ADMINISTRATION HOSPITAL,
New York, N.Y., June 2, 1977.

Senator GEORGE MCGOVERN,
Select Committee on Nutrition and Human Needs,
Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you for your letter of May 2 in which you ask me to comment on your committee's publication "Dietary Goals for the United States" as well as the supporting material you enclosed. I appreciate the complexities involved in setting up guidelines for a national diet policy. While I would accept that your publication follows a consensus of physicians throughout the world, I respectfully submit that many of the recommendations are premature and are not sufficiently established in fact to warrant the problems that would occur were they to be implemented on a national scale.

I have enclosed an article I was invited to write in 1973 for a publication that deals specifically with controversial issues in medicine. I have attached a copy of the title page so that you can obtain the volume and review the articles pertinent to this subject. These articles appear on pages 197-245 and include my own contribution which I have attached. I have seen no new information in the interval between my writing the article 4 years ago and the present that would lead me to make important changes in its substance or any changes in my conclusions. I am certain, however, that this is also true of those who expressed opposing points of view.

In addition to the points raised in the article, it is important to emphasize that, as your committee is well aware, there are serious nutritional problems that affect many Americans that are clearly related to dietary inadequacies particularly of high quality protein and are unrelated to dietary inadequacies particularly of high quality protein and are unrelated to the whole issue of atherosclerosis. Full implementation of your recommendations could have a negative effect on these problems, in that presently available sources of cheap protein might become less readily available and more expensive. The clearest example of this relates to limitation of cholesterol intake, a recommendation that would require marked decrease in egg consumption. As pointed out in your Table 5 (Protein Cost), eggs at \$.40 per day's allowance are one of the cheapest sources of protein available in this country. Are

we really sure enough that eating eggs leads to any disease to accept the far reaching nutritional and economic effects of their interdiction?

I should also like to raise questions about the validity of medical consensus, in the absence of experimental data, as a basis for national policy. As should be the case among flexible persons, today's consensus, based on the best available indirect evidence, is justifiably discarded as our base of information grows. Many were quite certain in the 1950's and 1960's (pages 10 and 11 of my article) that the hormone estrogen, should decrease heart attacks and it was given to many patients. Yet, today considerable evidence, including the National Heart Institutes Cooperative Study on cholesterol-lowering drugs, makes us consider estrogen an agent that increases the risk of such disease and the recommendation is to avoid its use. Similarly, as can be seen in the evolution of the recommendations made by the American Heart Association, the percent of polyunsaturated fat recommended to prevent heart disease has been decreased several fold in the past decade.

Finally, I should like to reemphasize the point made in the last paragraph of my enclosed paper. The use of national resources to establish health programs, including congressional recommendations, should be focused on those issues in which the case is convincing. We have strong support for the contention that treatment of high blood pressure and decreased cigarette smoking will decrease strokes and heart attacks (and in the case of cigarettes, many common malignant diseases). Is it really correct to diffuse what should be a concentrated and vigorous effort against these two risk factors by making recommendations about diet that will not have sufficient basis to be convincing and which will have serious economic implications, if implemented?

Incidentally, I recently received a letter indicating that my name was referred to you by the National Live Stock and Meat Board. I have never previously heard of this organization and I have no association with them. Any parallels between their views and mine are strictly coincidental.

Sincerely,

NORTON SPRITZ, M.D.,

*Professor of Medicine, NYU School of Medicine,
Chief, Medical Service, New York VA Hospital.*

SHALL WE RECOMMEND CHANGES IN DIET ON A NATIONAL SCALE TO PREVENT ATHEROSCLEROTIC DISEASE?*

(A skeptical view—Norton Spritz, M.D., Chief, Medical Service, New York VA Hospital, and Professor of Medicine, New York University School of Medicine)

Considerable indirect evidence suggests that the occurrence of atherosclerotic disease could be decreased in the United States were we to institute changes in the pattern of national food intake. This body of evidence has led to several recommendations for extensive alterations of the nation's diet. Such large scale changes in a nation's diet have serious economic and biological implications and require for their justification at least three conditions: the disease process to

*Controversy in Internal Medicine, II, W. B. Saunders Co., 1974.

be prevented has to represent a very extreme health risk to the population; the role of diet in its genesis has to be established by a large body of consistent evidence; and finally, the nature of the dietary deletions and/or additions likely to produce the desired effect has to be clearly established. In considering these criteria for a national diet policy for the prevention of atherosclerotic disease, the first requirement is certainly met. In my view, however, sufficient doubt exists concerning the other two to make unwarranted at this time a recommendation on a national scale.

One type of information that supports the idea that if we ate differently we would have less vascular disease derives from comparisons of dietary intake among population groups with different rates of atherosclerotic disease. The most recently published study¹ of this type is a carefully executed survey of the eating patterns and other environmental factors among men in seven population groups that have a wide variation in the occurrence rate of coronary heart disease. As has been less rigorously shown in other studies, there is a close association between the percent of dietary intake as saturated fat, the plasma cholesterol concentration and the prevalence and incidence of cardiovascular disease among these seven groups. Deaths from all causes, however, showed a far less clear association with saturated fat intake. The Japanese, Italian and American groups had comparable overall death rates, but their intake of saturated fat varied from 3 to 18 percent of total calories—essentially the entire range of the seven groups under study.

In addition to uncertainties about the relationship between diet and overall death rates among nations, there are other questions about the relevance of studies of different populations to recommendations for dietary change in a single population. These questions relate both to methodological and substantive problems. The methodological problems are the obvious ones concerning the reliability of the information about diet and the basis for the diagnosis of specific manifestations of vascular disease as well as the effects of other diseases on the findings. The use of death rate as the criteria for interpretation of these studies minimize the problems of diagnostic differences among nations. Also, death rate is the end point most meaningful if one is to use such data to support the contention that we should alter the American diet in a way to mimic that of countries with apparently less atherosclerotic disease.

In addition to methodological uncertainties, serious substantive questions exist about the applicability of these findings to recommendations for changes in our own diet. Recommendations based on this type of information are based on the assumption that environmental factors that are important in atherogenesis in one culture are equally important in another. Direct evidence exists indicating that this assumption may not be true. The striking importance of cigarette smoking as a risk factor for coronary artery disease has been repeatedly established in the United States.^{2,3} Yet in many other countries with

¹ Coronary Heart Disease in Seven Countries. American Heart Association. Monograph No. 29, 1970. Ancel Keyes, Editor.

² Doyle, J. T., Dawloen, T. R., Kannell, W. B. et al. The relationship of cigarette smoking to coronary heart disease. *JAMA* 190:886, 1964.

³ Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service. U.S. Dept. of Health, Education and Welfare, Public Health Service Document No. 1103, 1964.

both low and high incidences of vascular disease, smoking is unrelated to such disease.¹ This discrepancy among nations remains unexplained, but provides serious reservations about the validity of altering an environmental factor as a preventative measure in one country on the basis of its correlation with vascular disease among different population groups.

Even more direct evidence exists that dietary factors, which may correlate among nations with their rates of vascular disease, are not important determinants of disease within a single country. Within a single population group, differences in dietary intake has not been identified, in any instance, as a correlative factor with the risk of vascular disease. For example, in a prospective study of the diets of approximately 1000 people in Framingham, Mass.⁴ neither cholesterol content, the amount or type of fat nor total calories were different in those who did and did not develop coronary heart disease during the eight year study period. In sum, this and similar studies fail to support the idea that dietary intake plays an important role in determining risk of vascular disease.

This conclusion has been attacked on the basis that all members of populations like that of Framingham, Massachusetts, have a similar and excessively high intake of cholesterol and saturated fat and for that reason, a selective effect of diet can not be established. While this contention may be true, there is within that population a wide range of plasma cholesterol concentrations (from approximately 150 to 300 mg percent) with an associated 3-fold difference in risk of developing coronary heart disease between those with the highest and lowest levels. This wide variation in cholesterol concentrations, with its concomitant variation in risk of heart disease forms the very basis for the recommendation to lower plasma cholesterol. Yet, the best information available today indicates that this variation in cholesterol concentration results from factors other than diet and does not provide support for the contention that a cholesterol-lowering diet would affect the occurrence of vascular disease.

Of all sources of information, perhaps most pertinent to the question of a national diet recommendation is the group of investigations in which diets have been manipulated in order to determine whether such alterations affect the occurrence of vascular disease. I should like to focus consideration in this discussion on three such studies, each of which has been carefully carried out over a long period, and each of which is generally considered to support the idea that diet alterations will prevent vascular disease. In at least two of the three, that of Dayton et al in Los Angeles⁵ and Leren in Norway⁶ a similar pattern emerges—subjects receiving the cholesterol lowering diet had an apparently lower incidence of new vascular disease, but with no significant effect (for 8 and 11 years in the two studies) on total mortality.

For several reasons, mortality, rather than incidence of new manifestations of atherosclerotic disease, is the critical determinant when one considers these studies in relationship to the question of a national

⁴ Kannel, W. B. and Gordon, T. U.S. Dept. of Health, Education and Welfare. The Framingham Study. Sec. 24. The Framingham Diet Study: Diet and the Regulation of Serum Cholesterol, 1970.

⁵ Dayton, S., Pearce, M. L. et al. A controlled clinical trial of a diet high in unsaturated fat. *Circulation* 40, Suppl. No. II, 1969.

⁶ Leren, P. The Oslo Diet-Heart Study; 11 year report. *Circulation* 42:935, 1970.

dietary recommendation. Apparent effects of the dietary manipulation on parameters other than mortality are more subject to uncertainties that derive from differences in experimental design and diagnostic criteria. This problem in interpretation of morbidity data is pointed up by distinct qualitative differences in the protection afforded by the diet in the treatment of groups in the two studies under consideration. In the Norwegian study, the occurrence of angina was lower in the treatment group and provided the bulk of data supporting the idea that diet protected against heart disease. In the Los Angeles study, on the other hand, there was no effect on this manifestation of heart disease. In the Norwegian study, protection was shown in subjects who had a myocardial infarction prior to their entry into the study; in the Los Angeles study, those with prior vascular disease obtained no protection from the diet. In fact, the most clearly similar finding between these two studies, which together involved a total of over 1,000 men followed for from 8 to 11 years, was that at no time in either study was the death rate in the treated group less than that in controls.

The most recently published study⁷ is of a different design in that the study groups were institutionalized in two hospitals and the cholesterol lowering diet was administered to the patients in one hospital and then, after six years, the other. Comparisons were then made for each hospital between its control and experimental period. While in this study the incidence of new coronary heart disease and mortality from heart disease were found to be lower during the experimental periods, total mortality was not affected at all in women and insignificant in men.

The inability to convincingly alter total mortality in the large number of persons involved in these studies requires very careful consideration before making a national diet recommendation. In two of these studies, the subjects were middle-aged and older men with and without evidence of ischemic heart disease—a group in which any significant effect on atherosclerotic disease should have been reflected by decreased mortality at some time during the study. In the study in Los Angeles, the deaths from vascular disease that were apparently prevented by diet were offset by an increase in deaths from neoplastic disease. This observation was not borne out in a compilation⁸ of five studies in which dietary alterations had been carried out, but the compilation also showed that, even when large numbers are analyzed together, a significant effect of the cholesterol lowering diet on mortality is not seen.

The uncertain effects of diet alteration on total mortality stands in contrast to studies in which other risk factors, notably smoking and hypertension, have been manipulated. Essentially without exception examinations of overall mortality in ex-smokers shows their rates to be lower than that in current smokers and similar to those who have never smoked.⁹ The differences in mortality between the smokers and non-smokers are several-fold and are independent of blood pressure or plasma cholesterol concentration. Similarly, in a study of the effect

⁷ Miettinen, M., Turpeinen, O. et al: Effect of cholesterol-lowering diet on mortality from coronary heart disease and other causes. *Lancet*, II, 835, 1972.

⁸ Ederer, F., Leren, P. et al. Cancer among men on cholesterol-lowering diets. *Lancet* II, 203, 1971.

⁹ Kahn, H. A.: The Dorn study of smoking and mortality among U.S. Veterans: Report on 8½ years of observation in Haenszel, M., Ed. *Epidemiological Approaches to the Study of Cancer and other Diseases*. National Cancer Institute Monograph No. 19, p. 1-125, 1966.

of treatment for five years on moderate hypertension involving 380 men, total mortality in the untreated group was more than twice that in the treated group.¹⁰

Like those concerning cholesterol-lowering diets, the studies of changes in smoking and blood pressure may not be considered conclusive. They do, however, provide considerably more evidence than do the studies on diet that programs on a national scale aimed to decrease smoking and to treat hypertension would result in favorable effects in mortality. It is certainly possible that more studies in which diet is manipulated would provide a similarly stronger basis for a national diet policy. Even more likely, diet alterations instituted earlier in life might have an important effect on the death rate. Yet, given the data available today, at the very least it is evident that recommendation to the population that they stop smoking cigarettes and that they participate in a program to detect and treat hypertension can be made with considerably more assurance than those concerning diet.

Interpretation of diet studies and considerations of a national diet recommendation are confounded further by uncertainties about the composition of an ideal diet. Decrease in saturated fats, increase in polyunsaturated fats, decrease in cholesterol in the diet can all be shown to decrease plasma cholesterol concentration. In general, available evidence suggests that the diet changes are additive in their effect on plasma cholesterol concentration. In the diet studies cited above, all these alterations were utilized in the experimental diet. Present recommendations focus on decrease in saturated fat and a decrease in dietary cholesterol with only modest increase in polyunsaturated fats. This decrease in cholesterol lowering potential in the presently recommended diet from that used in diet trials makes these trials an even less certain basis for the proposed national diet recommendations. The elimination of recommended changes in polyunsaturated fats as a part of a lipid-lowering dietary program derives from the fact that high polyunsaturated fat intake is not the dietary pattern of any large population group and its safety in the long term is yet to be established. While this precaution represents sound policy, it also weakens the cholesterol-lowering effect of diet programs and concomitantly at least in theory, its potential for the prevention of atherosclerotic disease. The effects on heart disease and overall mortality of diets with low cholesterol and decreased saturated fat (with only minor manipulation of the polyunsaturate content) is unestablished since well controlled studies specifically designed to investigate this question have not been carried out.

The magnitude of the fall in plasma cholesterol that would be seen as a result of a national program is also an important uncertainty. In most of the investigations in which small study groups have been given cholesterol-lowering diets in a controlled trial, decreases of 15-20 percent have been achieved in the treatment group. The quantitative effect of the removal of large amounts of polyunsaturated fat from the diet program remains unknown. In a large feasibility study carried out by the National Heart Institute,¹¹ the subjects were free-

¹⁰ Veterans Administration Cooperative Study Group on Antihypertensive Agents: Effects of treatment on morbidity in hypertension II Results in patients with diastolic pressure averaging 90 through 114 mm Hg. JAMA 213:1143, 1970.

¹¹ National Diet-Heart Study Research Group: Final Report. Circulation 37, Suppl. No. 1, 1968.

living and under less rigid control. The degree of change was considerably smaller, even with diets with high polyunsaturated content as well as low cholesterol and saturated fat intake. In fact, in that study, weight loss per se had an effect almost equivalent to that produced by qualitative changes in diet. The subjects receiving cholesterol-lowering diets whose weights did not change during the year of diet trial had only an 8.2 percent fall in cholesterol compared to 5.4 percent fall for those given a control diet, but in whom weight loss did occur. This study, which involved several thousand participants, provides little basis for a diet recommendation on a large scale for the lowering of plasma cholesterol other than a decrease in total caloric intake.

Finally, the focus of recommendations for an alteration in the national diet has been limited to plasma cholesterol without consideration of the importance of plasma triglyceride. Although the data has more uncertainties, it now seems clear that higher levels of triglyceride,¹² like those of cholesterol, are associated independently, with increased risk of vascular disease. It is also evident that elevation of plasma triglyceride as a finding that relates to increased vascular disease is as prevalent, or perhaps more prevalent, than are elevations of plasma cholesterol.¹³ The presently recommended cholesterol-lowering diets are quite different from those that would be recommended to the nation or to an individual were lowering triglyceride the goal of the dietary intervention. Decrease in total calories without specific qualitative changes might be the most important part of a program directed to the lowering of triglyceride. Carbohydrate restriction, either in toto or by the interdiction of specific sugars, has been shown to lower triglyceride and, although a controversial issue, deserves further trial as a tool for the management of hypertriglyceridemia and the prevention of vascular disease.

It is tempting to conclude, that in spite of all of the uncertainties outlined in this discussion, the established statistical association between plasma cholesterol concentration and vascular disease, and the ability to lower cholesterol by dietary means, together provide sufficient basis for a national diet recommendation even in the absence of more direct basis for such a decision. One needn't look beyond the area of prevention of atherosclerotic disease, however, for a recommendation, based on similarly convincing indirect evidence, that appears to be incorrect as more information has been accumulated. The higher incidence of vascular disease in men than in women; the loss of this differential in women after menopause; the effect of estrogens on lipoprotein patterns, taken together, provided a seemingly unassailable basis for recommendations for the widespread administration of estrogens to both men and post-menopausal women in order to prevent vascular disease. Some of the early trials of estrogen therapy produced data consistent with this recommendation. Yet, in the past two decades further support for that idea has not been obtained and, indeed, estrogen administration has produced apparent increase in

¹² Albrink, M. J. and Man, E. G. Serum triglycerides in coronary artery disease. *Arch. Int. Med.* 103:4, 1958.

¹³ Heinle, R. A., Levy, R. I., and Fredrickson, D. S. Lipid and carbohydrate abnormalities in patients with angiographically documented coronary artery disease. *Amer. J. Cardiol.* 24:178, 1969.

vascular disease,¹⁴ such that present recommendations caution against its use in patients with risk related to coronary heart disease.

This discussion should not be interpreted as a plea for inaction in the area of prevention of atherosclerotic disease. On the contrary, a major objection to the institution of a complex and expensive effort to change food intake and to alter patterns of food production on a national scale without adequate experimental support is that such an effort will divert and dilute efforts that should be expended on programs more likely to make an important impact. Such programs should include extensive campaigns to decrease cigarette consumption; to detect and treat hypertension; and to identify persons in whom elevations of cholesterol and/or triglyceride constitute major risk factors and to institute diet or drug therapy appropriate for their specific lipid abnormality.

VETERANS' ADMINISTRATION,
WADSWORTH HOSPITAL CENTER,
Los Angeles, Calif., May 19, 1977.

Hon. GEORGE MCGOVERN,
Chairman, U.S. Senate, Select Committee on Nutrition and Human Needs, Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you for providing me with a copy of your committee's publication entitled "Dietary Goals for the United States" and for the invitation to comment upon these issues.

I am not broadly expert in nutrition and can only claim expert knowledge in nutrition as it applies to atherosclerosis. In regard to that specific and major problem, I can endorse the recommendations of your publication. The main reservation I would have is that more radical dietary changes (i.e. more radical restriction of saturated fat and cholesterol) might very well be even more efficacious.

On page 36 of the report, reference is made to Dr. Osmo Turpeinen's study in Helsinki of the possibilities for primary prevention of ischemic heart disease by diet. Two other controlled primary prevention studies have been completed in this country, one recently by Dr. Ivan Frantz in Minnesota and an earlier one by my colleagues and myself at this institution. The latter has been published; the reference is "Dayton, S., Pearce, M.L., Hashimoto, S., Dixon, W.J., and Tomiyasu, U. (1969) A Controlled Clinical Trial of a Diet High in Unsaturated Fat in Preventing Complications of Atherosclerosis, American Heart Association Monograph No. 25, New York." Our own trial strongly suggested that a diet reduced in content of saturated fat and cholesterol was effective in reducing complications of atherosclerosis in men under the age of 65. Dr. Frantz' study, of which only an abstract has been published (*Circulation* 52, supplement 11, page 11-4, 1975) did not fully support our conclusions. It is possible that his less encouraging results were due to the fact that the study was about half the duration of our own.

Most of my relevant views about the problem are summarized in a relatively recent publication, a reprint of which is enclosed. I would

¹⁴ The Coronary Drug Project Research Group: The coronary drug project. Initial findings leading to modification of its research protocol. *JAMA* 214:1303, 1970.

modify its contents in one respect. On page 33, I referred to the possibilities that diets such as we used might stimulate the development of carcinomas. There are a number of reasons for diminishing concern about this possibility. First of all, our own observations were more suggestive of a "red herring" than a real effect. Secondly, no other trial of similar diets resulted in a similar observation. Thirdly, since that time we have carried out animal experiments (*Journal of Nutrition*, in press) which suggest that diets rich in polyunsaturated fat are not cocarcinogenic. The gallstone effect referred to on page 35 of the enclosed reprint is probably real, but can be regarded as a relatively minor side effect in comparison with the disease which we are hoping to prevent.

If I can be of further help to your committee, please let me know.

Sincerely yours,

SEYMOUR DAYTON, M.D.

Chief, Medical Service,

Professor and Vice-Chairman, Department of Medicine, UCLA.

Enclosure.

[*Progress in food and nutrition science*, vol. 1, no. 3, pp. 191-206. Pergamon Press (1975).
Printed in Great Britain]

NUTRITION AND ATHEROSCLEROSIS

(Seymour Dayton—Medical Service, Veterans' Administration, Wadsworth Hospital Center, Wilshire and Sawtelle Boulevards, Los Angeles, California 90073)

1. INTRODUCTION

Until well into the twentieth century, the history of nutrition research is a recitation of assaults on diseases of nutritional insufficiency. Diseases of surfeit were scarcely recognized; obesity is, to be sure, a disease of overnutrition, and there are other examples; but in the aggregate they were not known to constitute a major public health menace.

The past several decades have changed all this. Atherosclerosis has been known for centuries, and has been identified retrospectively in an ancient Egyptian mummy, but until the twentieth century its major complication, ischemic heart disease, ranked low among causes of death in all countries. Within just a few decades, ischemic heart disease has become epidemic in North America and western Europe: in the United States it accounts for one-third of all deaths, and together with other complications of atherosclerosis causes fully one-half of all deaths. Much of this mortality occurs during advanced age, but there is a tragically high incidence and mortality among men in their forties and fifties and significant mortality even earlier.

Successes in dealing with other major lethal diseases, particularly the infectious diseases, no doubt account for part of the increased prominence of atherosclerosis in our vital statistics. But most students of the problem believe that there has been a major, absolute increase in atherosclerosis; and that this has accompanied and resulted from rapid changes in food patterns and in the prevalence of cigarette smok-

ing. Western man eats much more animal fat than did his nineteenth century ancestors. The evidence incriminating this surfeit in causation of atherosclerosis is presented below.

2. DESCRIPTION OF THE DISEASE

Atherosclerosis is a disease which affects the innermost portion of the lining (tunica intima) of arteries and which ultimately invades the middle coat (tunica media). The lesion, known as an atheroma, consists of a collection of intracellular and extracellular lipid, accompanied by proliferation of cells, by accumulation of mucopolysaccharides, and by changes in the fibrous components of the arterial wall. The accumulating lipid is dominated by esterified cholesterol, particularly cholesteryl oleate. The other striking characteristic of lipid accumulation is that the accumulating phosphatide is mostly sphingomyelin, which is only a minor component of plasma phosphatide.

Concerning pathogenesis of the atheroma, two main theories are prevalent. The first holds that the lesion is initiated by infiltration of plasma lipids, presumably in the form of lipoprotein which accumulates in the subendothelial portion of the tunica intima; that this process is somehow followed by accumulation of unbound lipid, particularly cholesteryl oleate, which then incites the other changes. An almost equally popular hypothesis is the encrustation hypothesis. This is based on the supposition that there is a constant process of fibrin deposition and fibrinolysis going on at the luminal surface of the endothelium and that this process normally is in such balance that fibrin never accumulates detectably. It is suggested that under abnormal conditions small fibrin deposits (thrombi) do accumulate and that these then become covered by new endothelium which grows out to cover the luminal surface of the thrombus. Accumulation of lipid within this new lesion occurs by some unspecified mechanism. There is at present no sound basis for choosing between these hypotheses, both of which find partial but not convincing support from experimental and observational evidence. It is entirely conceivable that both processes are involved: i.e., that the lesion is initiated as a fibrin thrombus, but that the lipid enters from plasma, across the endothelium. Experimental models supporting such a combined mechanism have been described.

The initial lesion is thought to be a small, exclusively intimal accumulation known as a fatty streak, consisting primarily of lipid-laden macrophages known as foam cells within the intima. This is thought to progress by stages to a fibrous plaque, that is, a lesion still lipid-rich in which a great deal of connective tissue has proliferated, particularly over the juxta-luminal portion of the collection. At this stage, too, disruption of the internal elastic lamina has occurred so that the lesion now involves the tunica media.

A more elaborate formulation of pathogenesis of the atheroma is presented by Getz *et al.* (1969). The growing lesion bulges into the lumen, producing a visible excrescence on the endothelial surface. Its deleterious effects are manifested chiefly by obstruction. This may occur (particularly in small arteries) by proliferation of the atheroma itself, or by occurrence of occlusive thrombosis. The latter process, it appears, occurs almost exclusively in areas where the atheroma has become ulcerated. Rarer complications are embolization of atheroma contents from ulcerated lesions; weakening of the arterial wall with subsequent aneurysm formation and possible rupture; and calcification, which is generally viewed as a 'complication' but which is not in itself harmful.

Morbidity in atherosclerosis is not an all-or-none phenomenon. Affected individuals are symptom-free for many years and often for decades after the initial lesions appear. In the affluent countries of the Western world atherosclerosis is nearly universal in adult man, but most are symptom-free and many remain symptom-free throughout their lifetimes. Morbidity is related primarily to development of lesions to large size in critical locations (such as the coronary and cerebral arteries), where occlusion is particularly prone to occur and where occlusion of small vessels can have devastating effects.

The commonest initial complication of atherosclerosis is myocardial infarction ('heart attack'), due to occlusion of a coronary vessel. Occlusions in these vessels can also result in unheralded sudden death or in angina pectoris. Occlusion in the cerebral circulation results in cerebral infarction ('stroke') or transient ischemic attacks, and occlusion of leg vessels can result in either gangrene or in exertional pain (intermittent claudication).

3. BLOOD LIPIDS AND ATHEROSCLEROSIS

It is clear that there is a relationship between serum lipid concentrations and atherogenesis. There exists high suspicion, but something less than certainty, that this is a causal relationship. In worldwide epidemiologic studies concerning prevalence and incidence of atherosclerotic complications in various population groups, a wide range of incidence levels has been observed. In the main, well-studied population groups who have a low incidence of overt coronary heart disease manifest relatively low serum cholesterol concentrations (i.e., average concentration in adult men generally well below 200 mg/dl). In contrast, populations such as those of North America and western Europe having high attack rates of coronary heart disease are characterized by mean serum cholesterol concentrations well over 200 mg/dl in middle-aged men. A similar observation is recorded when individuals within a population are studied; that is, where population samples within single communities have been followed for many years, the coronary attack rate has been highest among those individuals whose serum cholesterol concentrations were highest (Fig. 1). (See also Kannel *et al.*, 1971.)

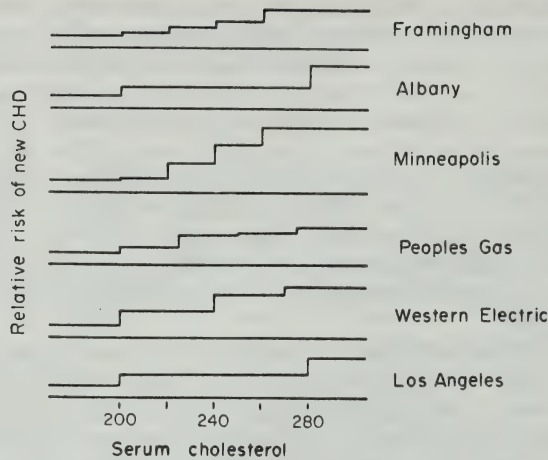


FIGURE 1.—Risk of developing ischemic heart disease (=CHD=coronary heart disease) in men in the United States as a function of serum cholesterol concentration in mg/dl. The data are taken from six prospective epidemiologic studies in which subjects had serum cholesterol levels determined during a baseline period and were then followed for a number of years. The ordinates are in arbitrary units, adjusted to similar levels in men with serum cholesterol levels below 200 mg/dl. (Data assembled by Stamler, J., "Lectures on Preventive Cardiology," New York, Grune & Stratton, 1967, p. 109.)

Actuarial records have established that overweight is associated with shortened life span, and prospective epidemiologic studies have demonstrated that severe obesity is one of the predictive precursors of ischemic heart disease. Men with excess body weight of more than 20 percent (as compared with the average at the same age and height in the same community) have almost twice the incidence of ischemic heart disease as do their less adipose neighbors (Fig. 2). This high incidence of cardiac disease accounts for much of the increased death rate among overweight individuals.

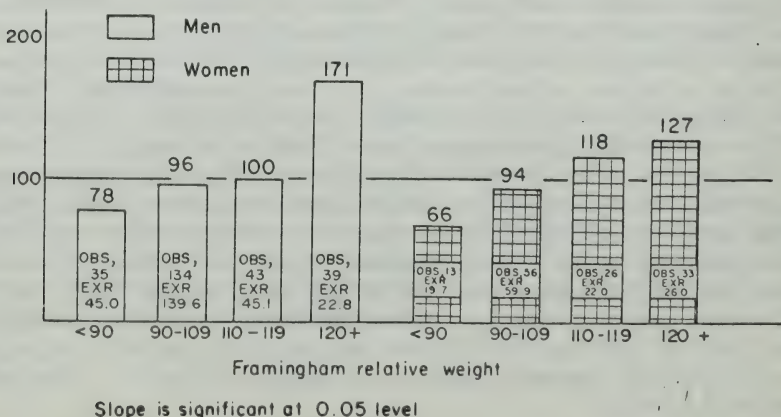


FIGURE 2.—The influence of overweight upon incidence of ischemic heart disease among middle-aged persons in Framingham, Mass., USA. 'Morbidity ratio' is 100 times the ratio of number of cases observed to the number expected; the latter figure was calculated by applying, in each sex, the age-specific incidence rates for the whole population to the subjects in the particular subgroup. 'Framingham relative weight' is 100 times the ratio of a subject's weight to the median weight for the same height and sex. (From Kannel, W. B., "Circulation" 35, 734, 1967.)

It is of interest and of considerable importance, however, that no serum cholesterol level, however low, is associated with total resistance to the disease. Similarly, no degree of leanness provides total resistance. Factors other than high serum cholesterol and overweight are certainly implicated in atherogenesis. The additional 'risk factors' already recognized include cigarette smoking, hypertension, diabetes mellitus, maleness, and perhaps sedentary habits and certain personality characteristics. Many of these operate at least in part through a tendency to be associated with high serum cholesterol levels. There is reason to believe that not all the risk factors have been identified.

While these relationships do not prove causality, information from other sources strongly supports the inference that high serum cholesterol has a casual role in the disease. First of all, as already noted; the lesion itself and particularly the early lesion is manifested by accumulation of esterified cholesterol. Secondly, laboratory animals (which generally have serum cholesterol concentrations lower than those of North American human adults) are ordinarily free of atherosclerosis, but the disease can be induced in these species by measures which elevate serum cholesterol levels. Some species are relatively sensitive to this type of induction and others more resistant, but none are totally resistant. Atheromata have been induced in more than a dozen species. In no instance has atherogenesis been induced by measures which fail to raise serum cholesterol concentrations; on the other hand, artificial elevations of serum cholesterol result in atheroma formation sooner or later in every species that has been thoroughly studied.

It is important to recognize that both environmental and genetic influences affect atherogenesis, and that the end result is consequence of the interplay and additive effects of these factors. For example, there are genetic disorders ('hyperlipidemias') in which serum cholesterol concentrations are extraordinarily high and in which susceptibility to atherosclerotic complications at early ages is also quite high. In some instances the abnormality is due to a monogenic familial disorder. However, among individuals without monogenic abnormalities, there exists a broad range of characteristic serum cholesterol concentrations even where environmental influences are identical. This appears to be due to polygenic influences (Goldstein et al., 1973b). But in all segments of the population, serum cholesterol concentration at a given time in a given individual is determined in part by environmental factors such as diet. It is thus wrong to view atherosclerosis purely as a genetically determined disease but equally wrong to view it simply as an environmental disorder.

It is profitable to consider what fraction of coronary disease victims are affected by one or another genetic hyperlipidemia. In the United States, familial hyperlipidemias appear to account for not more than 20 percent of coronary heart disease below the age of 60, and for a great deal less above that age (Goldstein et al., 1973a).

The role of hypertriglyceridemia in atherogenesis is less clear than the role of high serum cholesterol. Epidemiologic observations point to a definite correlation between serum triglyceride level and risk of atherosclerotic complications. However, there is a high intercorrelation between serum triglyceride and cholesterol levels, so that it has not been possible to demonstrate that serum triglyceride is an independent 'risk factor.' The only known form of 'pure' hypertriglyceridemia—i.e., elevated serum triglyceride with normal cholesterol—

is the type I defect (see below) or chylomicronemia; people with this disorder do not manifest unusual susceptibility to atherosclerotic complications. In contrast, 'pure' hypercholesterolemia (the type II disorder) is accompanied by extreme susceptibility to the disease. It thus seems entirely possible that the deleterious effects of high serum triglyceride are related to the fact that very low density lipoprotein also contains appreciable amounts of cholesterol, the serum concentration of which rises as endogenous lipoprotein accumulates in the very low density fraction.

4. RELATIONSHIP OF INDIVIDUAL NUTRIENTS TO ATHEROSCLEROSIS

Virtually all nutrients have been accorded some attention as to a possible relationship with the disease. Because the lesions consist predominantly of lipid and particularly cholesterol, dietary lipid and particularly dietary cholesterol have received earliest and most intense attention. In animal work it was established early in this century that dietary supplementation with cholesterol was capable of inducing atherosclerosis quite regularly and quickly in rabbits. The same is true of species such as the chicken. In still other species, however, cholesterol feeding must be augmented by additional nonnutritional manipulations. In the dog, induced hypothyroidism must accompany cholesterol feeding; in the rat, induced hypothyroidism plus addition of a bile salt to the diet. The disease induced in these species differs from the human disease in one way or another—most particularly, in limited involvement of the coronary arteries and failure to develop ischemic heart disease. But in some subhuman primate species, cholesterol feeding provokes ischemic heart disease manifested by myocardial infarction, mimicking the human disease.

In evaluating relationships of various nutrients to the human disease, two sources of information have been leaned on particularly heavily—first of all, data on characteristic nutrients in highly susceptible populations, and, secondly, experimental data on the manner in which various nutrients affect lipid concentrations and particularly serum cholesterol concentrations.

In international comparisons in which correlation between nutrient intake and incidence of coronary heart disease was sought, the most consistent correlation was the tendency of susceptible populations to consume large amounts of triglycerides rich in saturated fatty acids (mostly originating in meat and dairy products) (Keys, 1970). The typical North American, for example, consumes a diet in which fat provides more than 40 percent of caloric intake and in which the dominant sources of fat are beef and milk fat. In other parts of the world, however, fat consumption is either quantitatively or qualitatively quite different. For example, a Japanese population group with a low incidence of coronary heart disease was found to consume only 9 percent of its calories in the form of fat. In another area, the Greek island of Crete, total fat consumption is 39 percent of fat calories—nearly as high as in the United States—but it is dominated by olive oil, a fat with a high content of oleic (monounsaturated) acid. In this area, the incidence of ischemic heart disease (IHD) is every bit as low in Japan (Fig. 3). Both the Japanese diet and the diet of Crete are low in saturated fatty acids, as are diets in several other areas where the incidence of IHD is low (Fig. 4).

In similar comparisons, much weaker relationships have been found between cholesterol intake and incidence of ischemic heart disease; between total caloric intake and IHD incidence; between protein intake and IHD incidence; between monoenoic fatty acid intake and IHD incidence; between total fat intake and IHD incidence.

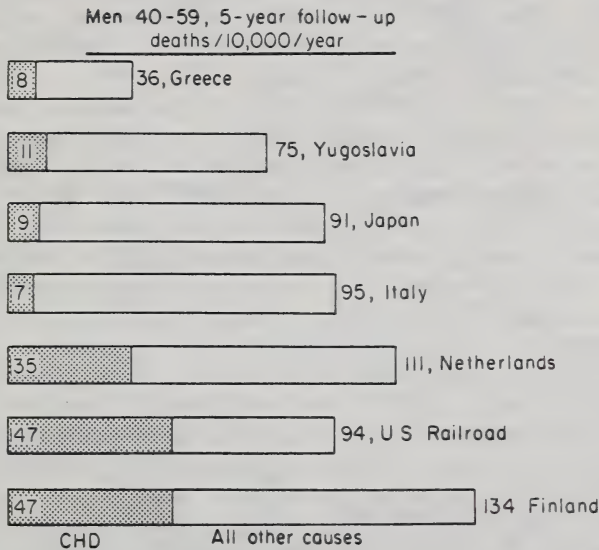


FIGURE 3.—Mortality due to ischemic heart disease (=coronary heart disease=CHD) and all other causes among defined male population groups in seven countries. A total of 12,770 men, aged 40-59 at the beginning of observation, were studied. The rates are age-standardized. Diets of the United States, Netherlands, and Finnish groups were substantially higher in saturated fat than were diets in the other four countries (cf. fig. 4). (From Keys, A., et al., American Heart Association Monograph No. 29, New York, 1970.)

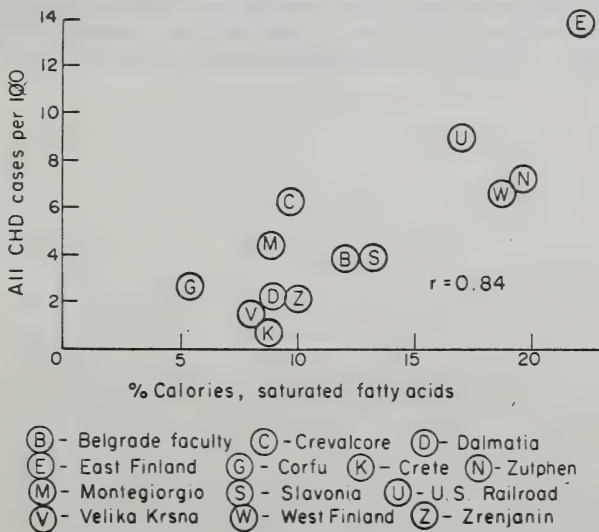


FIGURE 4.—Incidence of ischemic heart disease (=coronary heart disease=CHD) as related to saturated fatty acid intake. The data are from 5 years of observation of defined male populations in each of the 13 designated communities. Not included in the diagram is the Japanese community which appears in figure 3; its saturated fatty acid intake was 3 percent of calories. (From Keys, A., et al., American Heart Association Monograph No. 29, New York, 1970.)

Because of metabolic observations cited below, the experience of free-living human populations with diets rich in polyunsaturated fatty acids is of some interest. But in fact there has been little experience with self-selected diets of this type. Only the Burmese diet is known to have this characteristic because of liberal use of peanut oil in that country. But there have been no studies which would indicate whether the Burmese have experienced either beneficial or harmful effects from their high intake of peanut oil.

The effect of various nutrients on serum cholesterol concentrations of human subjects has been studied quite intensively over the past two decades. As recently as 1950 it was generally thought that edible fats were virtually indistinguishable from each other as to nutritional value, except for differences in essential fatty acid activity. During the 1950s, meticulous metabolic studies in human subjects demonstrated that this was not true in so far as serum cholesterol concentration is concerned. These studies were abetted by the introduction of liquid formula feeding, a technique which made it possible to modify fat intake without affecting other nutrients. It quickly became apparent (Ahrens et al., 1957) that there was a disparity between the effects of the common seed fats, which are generally rich in linoleic acid, and the body and milk fats of ruminants, in which saturated fatty acids dominate; substitution of seed fats (e.g., corn, cottonseed, safflower oils) for ruminant fats consistently induced decreases in serum cholesterol, the new levels being sustained as long as the seed fats were fed. Coconut oil—an exceptional oil in being highly saturated—had effects similar to ruminant fat (Fig. 5). Egg yolk lipid and heavily hydrogenated vegetable oils were found to have properties resembling those of ruminant fat; fish oils were found to resemble the seed oils; and the oils of seed coats (e.g., olive oil) were found to have intermediate properties.

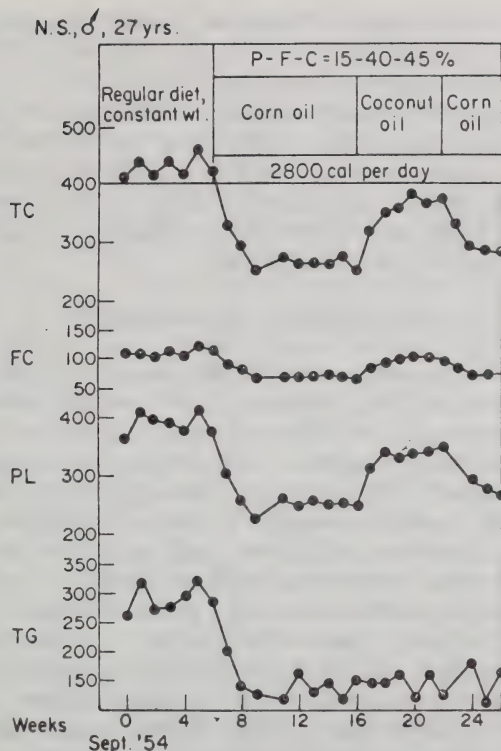


FIGURE 5.—An experiment in a human subject, demonstrating the difference between a highly saturated dietary fat (coconut oil; iodine value=10) and a highly unsaturated fat (corn oil; iodine value=126) in determining serum cholesterol concentration. The subject was a hyperlipidemic man, who after the sixth week was maintained on liquid formulas in which type of fat was the only variable; weight was kept constant throughout the experiment. TC=total cholesterol, FC=free cholesterol, PL=phospholipids, TG=triglycerides, all in mg/dl of serum. P-F-C=dietary protein, fat and carbohydrate, as percentages of total calories. (From Ahrens, E. H., Jr., *et al.*, *Lancet* i: 943, 1957.)

Studies with a wide variety of natural fats, hydrogenated fats, and highly purified materials have helped establish which components in these relatively complex mixtures are responsible for the observed effects. The dominant influences appear to be intake of saturated fatty acids and of cholesterol, which elevate serum cholesterol concentrations, and intake of polyunsaturated fatty acids which lower the serum cholesterol concentration. Relationships of these three nutrients to serum cholesterol have been summed up (Keys *et al.*, 1965) in a regression equation of the following form:

$$\Delta C = 1.2(2\Delta S' - \Delta P) + 1.5\Delta Z.$$

In this equation C is the serum cholesterol concentration; S' stands for glycerides of saturated fatty acids of 12–16 carbon atoms, as percentage of total dietary calories; P represents glycerides of polyunsaturated fatty acids as percentage of total dietary calories; and Z is the square root of dietary cholesterol in milligrams per 1,000 cal. The implications of the equation are these: as saturated fat in the diet is increased serum cholesterol will go up; as polyunsaturated fat in the diet is increased serum cholesterol will go down, and gram for gram the influence of saturated fat is twice as great as the influence of polyunsaturated fat. The magnitude of the dietary cholesterol influence is less readily summarized. The main conclusion about this nutrient was that modest decrements in dietary cholesterol induce trivial changes in the serum level (Keys *et al.*, 1965). More recent work suggests a somewhat more important role for dietary cholesterol (Mattson *et al.*, 1972). A significant reduction can certainly be induced by *rigorous* restriction of cholesterol intake (in persons previously consuming “western” diets), but the decrement which can be achieved through this measure in large numbers of free-living individuals is probably no greater than that achieved by liberal increase of polyunsaturated fat. In summary, then, the most important dietary determinant but not the only determinant of serum cholesterol concentration in the human is the amount of saturated fat.

The Keys equation omits terms for monounsaturated fatty acid and for stearic acid (18 carbons, saturated). These fatty acids appear to be similar to each other, and similar to equicaloric amounts of carbohydrate, in their effects on serum cholesterol concentration—i.e., they are neutral. No doubt the equation cited above is an imperfect statement of the relevant relationships, but it is almost certainly a reasonable and useful approximation.

Mechanism of the unsaturated fat effect is not yet totally certain. In some subjects, at least—generally normal individuals—substitution of highly unsaturated for saturated dietary fat results in augmented loss of sterols and bile salts into the feces. This mechanism has not been regularly demonstrable in hyperlipidemic individuals, even though their serum cholesterol levels are equally responsive.

Caloric balance appears to have little lasting effect upon serum cholesterol concentrations. Persons losing weight (whether by dietary restriction or by severe exercise) experience falls in serum cholesterol concentration, and persons gaining weight experience rises. However, these changes are transitory and are followed by return to the previous cholesterol level as soon as weight has stabilized at the new level.

For reasons discussed elsewhere, the influence of dietary factors upon circulating concentrations of endogenous triglyceride are also of

interest here. The influential factors are three. First of all, caloric balance: overweight people have on the average higher serum triglyceride levels than lean people. Weight reduction (by either caloric restriction or by exercise) is accompanied by lowering of serum triglyceride, and the reverse occurs during weight gain. Secondly, carbohydrate intake: high carbohydrate intake is accompanied by high fasting levels of circulating endogenous triglyceride. (This is probably relatively transitory, persisting through only a few weeks or months after a change in dietary habits, and therefore very likely has little influence on triglyceride concentrations in nonmutated persons who habitually consume high carbohydrate diets throughout their lives.) This effect of high carbohydrate intake is a normal phenomenon, which can be demonstrated regularly in normal people provided caloric balance is maintained. It is presumably a manifestation of the fact that chylomicra (which transport exogenous triglyceride) constitute a more favorable substrate for lipoprotein lipase than does very low density lipoprotein (which transports endogenous triglyceride). The phenomenon occurs in exaggerated form in type IV hyperlipidemia, which is described below. The third influence upon serum triglyceride is the type of dietary carbohydrate: dietary sucrose provokes higher endogenous triglyceride concentrations than does either dietary starch or dietary glucose taken in similar amounts (Kaufmann et al., 1966). This effect appears to be due to the fact that starch yields only glucose on hydrolysis, whereas sucrose yields equal quantities of glucose and fructose. Fructose is converted more readily into endogenous triglyceride than is glucose. The nature and amount of dietary carbohydrate have little influence, however, upon serum cholesterol concentrations.

The above comments refer to dietary influences on fasting serum triglyceride concentrations. But, of course, fasting conditions prevail during only a minor fraction of an individual's lifetime. Postprandial concentrations of triglyceride might be a good deal more important, but they have received less attention. Rises in serum triglyceride—both as chylomicra and as very low density lipoprotein—follow meals rich in fat, and rises in very low density lipoprotein triglyceride occur after large meals in which carbohydrate predominates. Similar comments do not apply to serum cholesterol; its level varies little through the day, regardless of food intake; such changes as do occur are largely inverse to changes in plasma volume.

Increased consumption of hydrogenated vegetable oils as margarines and shortenings has drawn some attention to the nutritional properties of trans fatty acids. The naturally occurring unsaturated fatty acids have double bonds of the *cis* configuration. Commercial hydrogenation results not only in hydrogenation of some unsaturated centers, but also in geometrical isomerization to *trans* configuration at some of the surviving double bonds. Trans fatty acids appear in the main to be free of noteworthy favorable or harmful effects. Compared with their *cis* counterparts, they elevate serum triglyceride levels to a modest degree. Considering the choice between butter, on the one hand—with its highly saturated fatty acids and some cholesterol—and conventional or 'unsaturated' margarines, present evidence favors the margarines despite their trans fatty acid content.

Dietary protein intake is probably not an important influence in the human disorder. In animal experiments protein restriction is capable of enhancing induced hypercholesterolemia and atherosclerosis.

This does not appear to be an important phenomenon in humans; in international comparisons there is no demonstrable relationship between characteristic dietary protein intake and susceptibility to atherosclerosis. Indeed, studied populations vary little (10–14 percent of calories) in their characteristic protein intakes.

β -Sitosterol, a poorly absorbed plant sterol, interferes with intestinal absorption of cholesterol. The effect requires ingestion of large doses of sitosterol—many grams per day. Since sitosterols are abundant in vegetable oils, there have been suggestions that they are responsible for the serum cholesterol-lowering effect of these oils. This is probably not the case, for even extremely liberal intakes of the common seed oils would provide sitosterol intakes less than one gram per day.

Ethanol intake, too, is not an important influence. Humans dying of ethanol-induced hepatic cirrhosis are found at autopsy to have less atherosclerosis than nonalcoholic persons of the same age and sex in the same population. This seeming protection, however, is not enjoyed by persons who consume alcohol liberally but who fail to develop cirrhosis. A small fraction of the population develops severe endogenous hypertriglyceridemia after ethanol intake; it is conceivable that this is deleterious in accelerating atherogenesis, but such an inference is entirely speculative.

Caffeine and coffee may provoke mild elevations in serum triglyceride concentration by stimulating lipolysis in adipose tissue cells; the free fatty acid thus released induces increased triglyceride synthesis by the liver, thus re-emerging into the circulation as very low density lipoprotein.

There have been many suggestions that atherosclerosis might be a manifestation of essential fatty acid (EFA) deficiency, but this hypothesis is probably in error. It arose largely out of the demonstrations, in the 1950s, that liberal intake of polyunsaturated fatty acid was capable of lowering serum cholesterol concentrations. Two considerations militate against the conclusion that essential fatty acid deficiency is responsible for the human disease. First of all, studies with fish oils having high iodine value but low EFA activity have demonstrated that they lower serum cholesterol concentrations about as effectively as do vegetable oils of high EFA activity. Secondly, there has been no reason to believe that low intake of vegetable oil or of essential fatty acids is characteristic of populations highly susceptible to atherosclerosis; and there is no evidence that nonsusceptible population groups consume large amounts of essential fatty acids.

The influence of mineral intake upon atherosclerosis has also been studied. The most interesting observation has been epidemiologic demonstration of the inverse relationship between water hardness and incidence of atherosclerotic complications. Although the relationship is well established, causality has not been established; the responsible component of hard or soft water (if any) has not been identified; and mechanism is in general quite obscure.

There has been no substantial evidence for a role of hypo- or hypervitaminosis in atherogenesis.

High intake of pectins has been found to lower serum cholesterol levels slightly. The effect is sufficiently small as to indicate that it cannot be an important factor in determining susceptibility to atherosclerosis in the individual eating ad libitum, and that it has little potential for prophylaxis or therapy.

5. DIET AND BLOOD COAGULATION

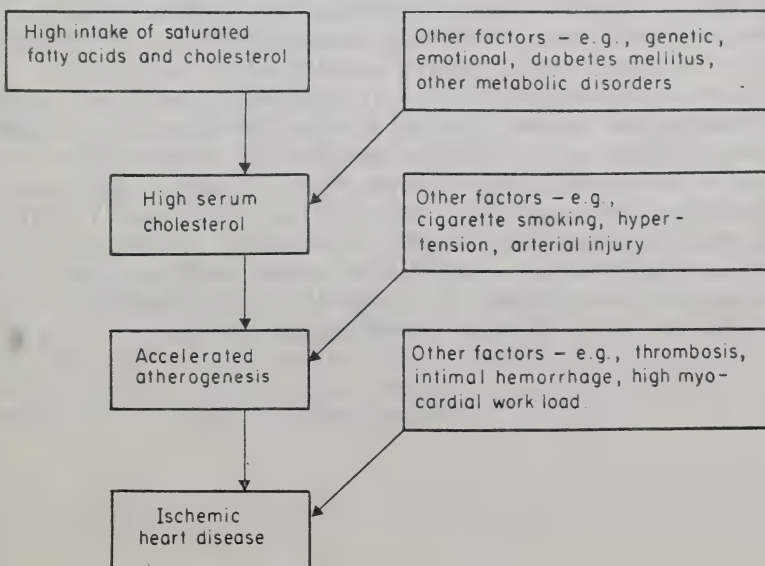
Since blood coagulation is perhaps involved in pathogenesis of the human atheroma, and surely involved in genesis of its clinical complications (Mustard et al., 1963), effects of nutrients upon coagulation might have some influence upon development of atherosclerosis. Clotting of blood is in fact accelerated during absorption of meals rich in fat, and this phenomenon is more pronounced when the meal contains predominantly saturated rather than unsaturated fat. It is doubtful, however, that the nature of one's habitual dietary fat ordinarily has much impact on coagulation in the postabsorptive state.

An interesting phenomenon, of uncertain importance in this context, is the effect of salts of long chain fatty acids in initiating (and thereby accelerating) coagulation. Saturated free fatty acids, when present as soaps, activate either Hageman factor or plasma thromboplastin antecedent, and can thus provoke very rapid coagulation. This does not occur, however, when the free fatty acid is bound to albumin, as is surely the case under normal physiologic conditions. Under certain extreme laboratory conditions, however, free fatty acids may circulate in massive concentrations and provoke intravascular coagulation, perhaps because some of the FFA fails to become bound to albumin. It is not known whether this ever occurs in humans. If it does occur, intakes of diets rich in unsaturated fat would presumably be advantageous, since unsaturated fatty acids are much less effective than saturated fatty acids in initiation of clotting.

Such phenomena may explain the fact that diets rich in saturated animal fat are thrombogenic in some animal species. Similar effects in human subjects have not been established.

6. ATTEMPTS AT DIETARY PREVENTION OF HEART DISEASE

As noted earlier there is a large body of evidence supporting the following hypothesis concerning pathogenesis of ischemic heart disease:



Support for a causal role of these dietary factors is, however, not yet fully convincing, and for this reason it is not totally certain that dietary modification is capable of preventing or retarding the disease. As an important corollary, if these dietary modifications are in fact capable of retarding or preventing the disease, it is not certain at what stage of life the effort at cholesterol lowering must be undertaken.

It is reasonable to hope that return (in the Western world) to the more ascetic dietary habits prevalent among less complex cultures would reverse the environmental contribution to blood lipid elevation and prevent, or at least retard, atherosclerosis. However, low fat diets are poorly accepted among persons conditioned by a lifetime of fat-rich and varied foods. For this reason, most efforts at nutritional prevention of IHD have employed diets rich in unsaturated fat.

The prevention question is best considered under two subheadings—primary prevention and secondary prevention. The former refers to prevention of complications in the individual who has not yet suffered an overt complication of atherosclerosis. Secondary prevention, on the other hand, refers to prevention of new complications in individuals who have already sustained and survived clinically overt manifestations of coronary heart disease.

A number of experimental attempts at secondary prevention through modified diet have been undertaken and completed (reviewed by Dayton, 1970). The best of these have involved dietary lowering of serum cholesterol by decreased intake of saturated fatty acid and cholesterol and by augmented intake of vegetable oils rich in polyunsaturated fatty acid. The outcome in the most rigorously controlled studies suggests that a subject modifying his diet may expect to experience a small decrease in risk of new events but little prolongation of life. There seem to be benefits, but it is uncertain that they are of sufficient magnitude to justify the effort.

Primary prevention is basically of more importance than secondary prevention because many persons fail to survive the initial attack; the number dying instantaneously or within the first few hours is at least 15 percent and perhaps as high as 40 percent. Efforts at primary prevention have yielded encouraging but still not definitive results. There have been several trials involving restricted intake of dietary saturated fat and cholesterol and augmented intake of polyunsaturated fat in the form of vegetable oils. These studies have produced results distinctly favoring a conclusion that such a diet favorably modifies the incidence of acute myocardial infarction and sudden death. Indeed, in one of these experiments (Dayton *et al.*, 1969) a beneficial effect appeared to ensue even among men in their advanced middle years (55–65 years of age) (Fig. 6). For one reason or another, however, none of the trials has been totally convincing, and they are not totally convincing in the aggregate. It is particularly noteworthy that none of the trials has demonstrated prolongation of life.

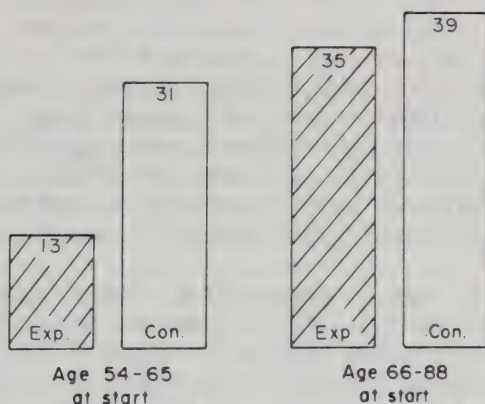
Deaths due to acute
atherosclerotic events

FIGURE 6. Mortality due to acute complications of atherosclerosis in a controlled clinical trial of diet low in saturated fat and cholesterol, and rich in polyunsaturated fat. The subjects were 846 domiciled male veterans who had been allocated randomly to experimental (Exp.) and control (Con.) diets and followed under double-blind conditions. Mean period of observation was 6½ years in both groups. Numbers on the bars indicate numbers of subjects dying of acute atherosclerotic complications during the trial. (From Dayton, S. *et al.*, *Ann. Intern. Med.* 72, 97, 1970.)

A troublesome and unsettled point has to do with the possibility of “toxic” effects of polyunsaturated fatty acids. In experimental animals these have augmented the incidence of induced carcinomas and, in at least one experiment, of spontaneous carcinomas. In one of the primary prevention studies in humans there was a suggestion of a similar effect (Dayton *et al.*, 1969). There is also evidence that such diets may induce gallstone formation (Sturdevant *et al.*, 1973). The question of safety requires considerably more study, particularly as applied to decades of exposure.

The most promising dietary approach to prevention of atherosclerosis is perhaps one which has received no attention whatsoever in clinical trials. As noted earlier, certain Greek population groups habitually consume a diet in which fat is provided liberally in the form of olive oil, and which therefore contains predominantly monounsaturated fatty acid (oleic acid). Middle-aged men in these populations were found to have the lowest all-causes death rates of any population studied thus far (Fig. 3). Such a diet would offer the relatively high fat intake which appears essential to acceptability among North American and European populations, and based on present information it might prove free of toxicity. It appears to deserve a clinical trial.

There have been no meticulous clinical experiments aimed at demonstrating the value of weight reduction alone in prevention of IHD, but there appears to be no controversy as to the desirability of correcting obesity by nutritionally sound measures.

7. THE ROLE OF DIET IN MANAGEMENT OF HYPERLIPIDEMIAS

There exist a number of disorders characterized by chronic, extreme elevation of serum lipid concentrations. Some of these are "secondary" in the sense that they appear to be symptomatic of an identifiable underlying disease such as uncontrolled diabetes mellitus, hypothyroidism, nephrotic syndrome, biliary obstruction, high ethanol intake, adrenal corticoid therapy, glycogenosis, and multiple myeloma. In all of these instances, therapeutic needs are directed toward control of the underlying disorder, and dietary measures to control the hyperlipidemias are rarely indicated (with a possible exception in the case of diabetes mellitus).

There are also a large number of individuals with chronic hyperlipidemias in which no underlying disease can be identified. These are referred to as "primary" or idiopathic hyperlipidemias; in most instances they are familial and due to a genetic defect. Dietary modification is a useful tool in their treatment. Five "phenotypes" are recognized following a classification scheme introduced by Frederickson et al., (1967) (Fig. 7), and these are briefly summarized below.

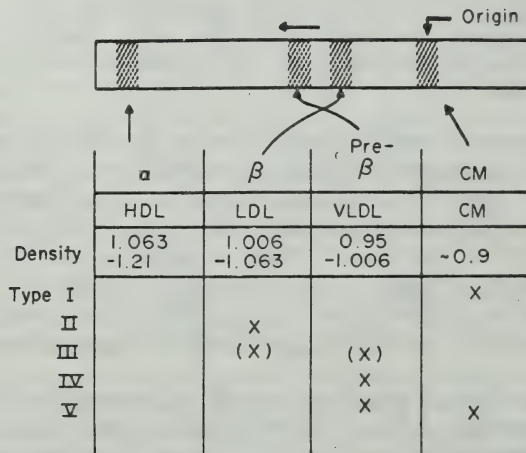


FIG. 7.—Nomenclature of lipoproteins and of the Frederickson classification of hyperlipidemias (hyperlipoproteinemias). At the top is a schematic representation of a paper electrophoretic strip run in albumin-containing buffer and stained for lipid. "Origin" designates the point of application, and the arrow above the middle of the strip indicates the direction of protein migration. Immediately below this are the names of the four main fractions: CM=chylomicra. Below this are the names generally applied to the same fractions when isolated ultracentrifugally; HDL=high density lipoprotein; LDL=low density lipoprotein; VLDL=very low density lipoprotein. On the next line are the densities of these fractions. The lower portion of the diagram indicates which fraction(s) is present in abnormally high concentration in each of the 5 phenotypes. A type IIb is recognized; β -lipoprotein is the dominant fraction, but there is some increase of pre- β as well. In type III, a single broad band extends across the β - and pre- β -regions.

Type I. These subjects have high concentrations of circulating chylomicra in the fasting state, and therefore have high fasting triglyceride concentrations and normal cholesterol concentrations. The defect is due

to absence or deficiency of lipoprotein lipase, the enzyme responsible for chylomicron lipolysis. Affected persons do not appear to be susceptible to premature atherosclerosis but in the severer forms may be afflicted by recurrent pancreatitis and by bouts of undiagnosable abdominal pain. Control of the serum lipid defect results in abatement of the symptoms. Two modalities are available: (1) a low fat diet, (2) a diet containing medium chain triglyceride (MCT) as the dominant source of fat. The fatty acids of chain length below 11 are transported from small intestine almost exclusively in portal blood, in the form of free fatty acid bound to albumin. They therefore do not provoke chylomicron formation, and for this reason metabolism of fat from MCT-containing diets is not dependent upon the lipoprotein lipase mechanism which is deficient in these individuals.

Type II. These subjects have a high concentration of serum low density lipoprotein (β -lipoprotein) and therefore have high serum cholesterol concentrations with normal or near-normal serum triglyceride concentrations. A type IIb is recognized: the accumulation of β -lipoprotein is accompanied by moderate increase in the pre- β fraction, and therefore by mild hypertriglyceridemia. Mechanism of the defect has not been established but there is evidence suggesting a defect in metabolism of the peptide of the lipoprotein complex.

Affected individuals are highly susceptible to premature atherosclerosis; by age 50, about half have already sustained overt manifestations of the disease. Partial or complete control can be obtained by dietary measures which lower β -lipoprotein concentrations: restriction of saturated fat and cholesterol, with or without supplementation of the diet by polyunsaturated fatty acids. Although dramatic responses to these diets are occasionally seen, lowering of serum cholesterol to a satisfactory level does not usually result; for this reason drug therapy is generally employed in addition to diet.

The disease can be recognized in umbilical cord blood at birth, the hallmark at this age being a serum cholesterol concentration over 100 mg/dl. Because of the seriousness of the uncontrolled disease, screening programs directed at the newborn are being undertaken.

Type III. The surplus lipids circulate as an abnormal lipoprotein which on electrophoresis migrates as a broad band in the β - and pre- β -regions; on ultracentrifugation the total band, including that portion migrating in the β -region, has a density less than that of serum and floats to the top of the tube. It is believed to be a "remnant" from hydrolysis of pre- β lipoprotein triglyceride—one which is undetectable in normal blood because of rapid further degradation to β -lipoprotein. The subjects, like those with type II defects, are susceptible to premature complications of atherosclerosis. Substantial decrements in serum lipid concentrations result from a diet similar to that used in the type II disorder—with, in the overweight patient, dietary caloric restriction as well.

Type IV. The defect is manifested as high fasting concentrations of very low density (pre- β) lipoprotein. On chemical fractionation the serum has high concentrations of both triglyceride and cholesterol but with the former predominating. The mechanism has not been established but appears to involve defective clearance of endogenous triglyceride from the bloodstream. These individuals, too, have a high incidence of premature atherosclerosis. Most of them are obese and

the chemical defect responds well to ordinary weight-control measures. It is also useful to substitute starch or glucose for sucrose in the diet. Low carbohydrate, high fat diets also control the chemical defect but probably ought not to be used because they induce marked post-prandial rises in plasma triglyceride.

Type V. Both chylomicra and very low density (pre- β) lipoproteins accumulate. The disorder is rare. Triglyceride elevation is most striking but there is some cholesterol elevation as well. A diet similar to that used for the type IV defect has been employed.

Of these disorders, two—types II and IV—dominate in terms of frequency.

While the above scheme appears to have some descriptive value, it is not clear whether it is uniquely useful as a guide to dietary or other treatment. The classification system was considered useful as a means of genotyping the hyperlipidemias, but more recent work indicates that a different approach, not requiring lipoprotein assay, may be superior for this objective. Goldstein et al. (1973b) have provided support for existence of the following entities:

- (1) Familial monogenic hypercholesterolemia.
- (2) Familial monogenic hypertriglyceridemia.
- (3) Familial combined hyperlipidemia (a monogenic disorder in which a given affected individual may be hypercholesterolemic, hypertriglyceridemic, or both).
- (4) Familial polygenic hypercholesterolemia.
- (5) Sporadic hypertriglyceridemia.

None of these entities corresponds consistently to a single lipoprotein phenotype. The Goldstein scheme takes no cognizance of familial hyperchylomicronemia (type I), which is certainly a separate entity, nor of "dyslipoproteinemia" (type III), which is probably a separate entity. The monogenic disorders appear in the aggregate to affect nearly 1% of the population studied (Seattle, Washington, USA). It is not known whether identification of the genotype, according to the Goldstein scheme, will provide an adequate basis for selection of dietary or other treatment.

7.1. Diet for the diabetic

Accelerated atherosclerosis is a major problem in the diabetic and accounts for most deaths among diabetic adults. The mechanism of this acceleration is uncertain, but several hypotheses concerning mechanism are compatible with available information and are deserving, therefore, of serious consideration:

(a) The low carbohydrate diets of recent decades, adopted with the objective of minimizing glycosuria, have resulted in unusually high intakes of saturated fat among diabetics, and the early atherosclerosis of the diabetic is therefore iatrogenic.

(b) Thickening of capillary basement membranes, which characterizes the diabetic state, may impair function of the vasa vasorum in such a way as to promote atherogenesis; perhaps, for example, the vasa vasorum provide a path for egress of lipoprotein from the normal arterial wall, and perhaps this exit is slowed by thickened basement membranes in this area.

(c) The hyperlipidemia which characterizes uncontrolled, insulin-dependent diabetes mellitus is the root of the problem. Insulin is in-

volved in several key reactions affecting movement of lipid between capillary plasma and adipose tissue. It is required for activation of lipoprotein lipase, which is responsible for clearing of chylomicron triglyceride and very low density lipoprotein triglyceride from plasma. Insulin is required for formation of α -glycerophosphate, without which the adipose tissue cell cannot synthesize triglyceride for storage. Insulin also inhibits the lipase of the fat cell, tending thereby to retain triglyceride in the storage droplet. The effect of insulin insufficiency at all three enzyme sites is to promote accumulation of triglyceride in plasma. The result is a type IV, type V, or occasionally type I defect. The accumulation of very low density lipoprotein is accompanied by serum cholesterol elevation, as a secondary phenomenon.

Which of these phenomena induce accelerated atherogenesis in the diabetic is not known; perhaps all three do so in combination, and perhaps other as yet unrecognized phenomena as well.

The best diet for the diabetic has not been established. It seems clear that glycosuria should be controlled by weight control where needed and by insulin or drugs, rather than by use of high fat, low carbohydrate diets. It seems prudent, but of undemonstrated value, to recommend that the diabetic limit his intake of saturate fat and cholesterol. Careful control of the lipid defects by insulin therapy seems logical, but its value in retarding atherogenesis is not supported by the limited experimental evidence available at this time.

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WASHINGTON UNIVERSITY,
SCHOOL OF MEDICINE,
LIPID RESEARCH CENTER,
St. Louis, Mo., June 2, 1977.

HON. GEORGE MCGOVERN,
Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: Thanks very much for sending me a copy of "Dietary Goals for the United States". I find myself in agreement with most of the points raised therein. Congratulations on a fine job.

Sincerely yours,

GUSTAV SCHONFELD, M.D., *Director.*

UNIVERSITY OF CALIFORNIA, BERKELEY,
DEPARTMENT OF NUTRITIONAL SCIENCES,
Berkeley, Calif., June 2, 1977.

HON. GEORGE MCGOVERN,
Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: This is in response to your recent letter asking me to comment on the February 1977 report of the Select Committee on Nutrition and Human Needs titled "Dietary Goals for the United States".

As you know I have been a consistent supporter of the work of your Committee and have testified on its behalf on several occasions. The reports of your Committee and legislation which has grown out of your Committee's work have played a very important role in improving the nutritional health of the American public. Much malnutrition has been averted and the health care bill of this nation is lower than it would have been otherwise without your fine work.

My comments deal most specifically with pages 12 and 13 (the proposed "Dietary Goals") along with some of the explanatory material. From over 38 years of experience as a nutritional scientist and biochemist involved in nutrition research in this entire period, and as one who has been much involved in nutrition training, education, and policy setting at the national level, I can say I agree quite wholeheartedly with your over-all dietary goals as outlined in the diagram in Figure 1 on page 12 of your report (but not in the written portion of this page). From here on, however, I have considerable disagreement.

I feel we do not have the evidence to accept all the specific "changes in food selection and preparation" given on page 13. Specifically, I do not agree at all with statement No. 2 (that we must decrease consumption of meat), of No. 4 (nonfat milk for whole milk), No. 5 (butterfat and eggs) or with No. 7 (reduce salt to 3 grams).

There is good evidence available that those who consume meat at the average level or more have as good health records and freedom from chronic diseases as people who do not. Though I feel people should trim the excess fat off meat when they prepare or eat it, meat is one of our time-honored best foods. Meat is a major contributor of vitamins, minerals, and protein to our diets.

I also think it equally wrong to recommend that our general public use nonfat milk and fewer eggs. Like meat, milk and eggs are among our best foods and we are a healthier nation because we have such good supplies. We need to consume more, not less.

Though I have given specific objections to your proposed food selection goals, I wish to object even stronger to the overall way in which you have come up with national "Dietary Goals" (based on what I consider very limited information from the testimony of a rather small number of selected persons not all of whom are trained or experienced in giving dietary advice to the American public).

Such issues as specific dietary patterns for our entire population are best developed by non-political national nutritional groups such as the Food and Nutrition Board, or better, an ad hoc Nutritional Goals Advisory Group (with a truly representative set of knowledgeable persons representing many branches of nutrition, health and medicine. This should include representatives from state universities, state and federal public health agencies, U.S.D.A., the private sector, consumer groups, and representatives of the various nutrition societies and groups, such as those which make up the National Nutrition Consortium.)

In summary, I feel that we do not need rigid, inflexible, dietary patterns in this country, nor do I think that a Congressional Committee should be the source of specific dietary advice.

I suggest the Report not be issued as it now stands, but only after deletion of the questionable portions. I feel the report should also recommend that some independent nutrition body of national stature come up with a flexible list of specific dietary patterns that the American public might follow if we are not satisfied with the basic "four food group" approach.

Thank you for this opportunity to comment.

Sincerely yours,

GEORGE M. BRIGGS,
Professor of Nutrition.

COLLEGE OF PHYSICIANS & SURGEONS OF COLUMBIA UNIVERSITY
New York, N.Y., June 1, 1977.

HON. GEORGE MCGOVERN,
*Chairman, Senate Select Committee on Nutrition and Human Needs,
U.S. Senate, Dirksen Senate Office Building, Washington, D.C.*

DEAR SENATOR MCGOVERN: This is in reply to your letter of May 2, 1977 asking for my comments on "Dietary Goals for the United States" as prepared by the staff of the Select Committee on Nutrition and

Human Needs. I have been out of the country and could not answer your letter before this.

I will confine myself to a discussion of arteriosclerotic heart and vascular disease to dietary fat and cholesterol intake, about which I have recently lectured in New York and abroad.

I believe that the recommendations of the Select Committee with regard to fat and cholesterol intake are a disservice to the health of the people of the United States. This opinion is explained in detail in the enclosed paper, parts of which have been published in various journals. It is my conviction that elevated serum cholesterol is a consequence, rather than the cause, of arteriosclerotic lesions. There is a hemostatic relationship between endogenous and exogenous cholesterol which tends to keep serum cholesterol constant so that dietary cholesterol is of no consequence for heart disease. Cholesterol is probably part of repair processes in the disease.

Reduction of serum cholesterol by drugs has turned out to be a complete failure. Reduction by dietary polyunsaturated fat does not seem to offer any advantage, as becomes evident if the literature on this subject is scrutinized carefully.

Increased intake of polyunsaturated fat may even present some hazards because they may increase tissue peroxidation. Furthermore, they may contain toxic substances, some of which may even be mutagenic. When polyunsaturated fats are made into margarines, large amounts of trans fatty acids are produced, the nutritional properties of which are not sufficiently known.

Although I am in favor of a low calorie, intelligently balanced diet, I deplore the recommendation that materials known only for the last few decades and of questionable safety should replace fats which we have been using for at least fifteen thousand years.

Very truly yours,

HANS KAUNITZ, M.D.,
Clinical Professor, Retired.

IMPORTANCE OF LIPIDS IN ARTERIOSCLEROSIS: AN OUTDATED THEORY

(By Hans Kaunitz, M.D., Department of Pathology,
Columbia University, New York, N.Y.)

Around the turn of the century, when biochemistry replaced morphology in etiological explanations of biological phenomena, alterations of lipid metabolism attracted more and more attention from workers interested in arteriosclerosis (as it was named by Lobstein in 1826¹). The fatty composition of the arteriosclerotic plaques (called 'atheroma' from the Greek word, *athere*, for gruel) and the high lipid content of the blood itself in many cases of arteriosclerosis were emphasized while other forms of arterial degenerative disease, such as Mönckeberg's media calcification² and arteriolar sclerosis of visceral arteries,³ found less attention. The atheromata attracted so much attention that, in 1904, Marchand suggested 'atherosclerosis' as a more

¹ Lobstein, J. F. "Traites d'Anatomie Pathologique" Levrault, Paris, 1833.

² Mönckeberg, J. G. Virch. Arch. Path. Anat. 171: 141, 1903.

³ Long, E. R. in Cowdry's Arteriosclerosis, H. T. Blumenthal, Ed. Charles Thomas, Springfield, 1967, p. 5.

appropriate term than arteriosclerosis.⁴ The name, atherosclerosis, readily found acceptance because it reflected the current ideas that disturbances of lipid metabolism were the cause of degenerative diseases of the arteries. Because so many of the theories behind present-day concepts of 'atherosclerosis' are controversial, it may be more unprejudicial in a discussion of the problem to return to the older 'arteriosclerosis'.

The number of scientific investigations of lipid changes related to arteriosclerosis has by now reached unmanageable proportions. However, I have tried to select some of the main facts which link cholesterol with arteriosclerotic changes:⁵

(1) The atheroma contains a large amount of cholesterol, a fact emphasized by many investigators.

(2) It has been shown over and over again that, on a statistical basis people with high serum cholesterol levels have a significantly higher incidence of myocardial infarctions. This has again been stressed in a recent report from the Royal College of Physicians of London.⁶

(3) Patients with diseases associated with elevated serum cholesterol levels (e.g., nephrosis) have more advanced arteriosclerotic lesions than normal persons.

(4) It has been shown many times that feeding of large amounts of cholesterol, especially in conjunction with fats of animal origin, is associated with the appearance of cholesterol deposits in the aortas of some species.

Although these facts lend themselves to several interpretations, the most widely accepted hypothesis is the lipid theory of arteriosclerosis which postulates that elevated serum cholesterol is causally related to the disease and that reduction of serum cholesterol is associated with improvement.

The lipid theory of arteriosclerosis, which many workers in the field believe to be—for all practical purposes—an established fact, is the basis for far-reaching dietary recommendations as to the total fat content of the diet, the kind of fat to be consumed, and the cholesterol content of the diet. Because the intake of unsaturated vegetable oils is associated with a drop in serum cholesterol, they are believed to be desirable.

The American Heart Association has recommended a restriction of fat intake from about 40 percent of calories to 30–35 percent and a daily intake of not more than 300 mg of cholesterol (instead of the usual 300 to 1000 mg). Furthermore, unsaturated oils should be increased to at least 10 percent of calories (instead of 5 percent) and saturated fats should be reduced.⁷ Recently, these recommendations were accepted by the Royal College of Physicians.⁶

Such recommendations would entail a radical change in the American diet. In Fredrickson's words, it would be the requiem for the egg; dairy products would largely have to be replaced by foods containing polyunsaturated fats.⁸

⁴ Marchand, F. Verhandl. Kongr. Inn. Med. 1904, p. 23 Leipzig.

⁵ Kaunitz, H. *Nature* 192: 9, 1961.

⁶ Prevention of Coronary Heart Disease. Report of a Joint Working Party of the Royal College of Physicians of London and the British Cardiac Society. *J. Roy. Coll. Physicians* 10: No. 3, 1976.

⁷ Diet and the Possible Prevention of Coronary Atheroma. A Council Statement. *J. Am. Med. Assn.* 194: 1149, 1965.

⁸ Fredrickson, D. S. *Brit. Med. J.* 2: 187, 1971.

However, it behooves us to consider other hypotheses for the development of arteriosclerotic lesions, especially in view of certain facts which do not fit in with the lipid theory. Among them are the following:

The earliest lesions are seen in infants and may even occur in utero.⁹ It is interesting that early plaques do not contain more cholesterol than the surrounding tissue.¹⁰ Furthermore, it is difficult to explain the spotty distribution of the lesions if one assumes that we are dealing with a generalized disturbance of lipid metabolism. It seems more likely that such a change in metabolism would have to involve the whole organ. On the basis of the lipid theory, it is by no means clear why the serum high-density lipoprotein fraction, which is related to cholesterol metabolism, is reduced in arteriosclerotic heart disease.^{11 12} (We will return to this later.) One could also cite the old, and never contradicted, reports that feeding of cholesterol increases resistance to infections.^{13 14} Furthermore, exercise increases serum cholesterol but, at the same time, is beneficial in preventing heart disease.¹⁵ And, finally, mother's milk contains a considerable amount of cholesterol.

A review of some facts about cholesterol metabolism may be helpful. The daily turnover of cholesterol in the body is 1000–2000 mg. The plasma turnover is approximately 1000 mg/day, and most of it is esterified with fatty acids. On centrifugation, a large part appears in the fraction of low density lipo-proteins, which correspond to the beta-lipoproteins obtained by electrophoresis.

Most of the body's cholesterol is endogenous, being produced mainly in liver and intestines. The usual American diet supplies 300–1000 mg of cholesterol/day, of which only about 150–300 are absorbed; this is true even with higher dietary levels. There has been a great deal of controversy about the influence of dietary cholesterol on plasma cholesterol levels, which is understandable from the point of view of the lipid theory. By now, it seems to be well established that there exists a homeostatic relationship between dietary and endogenous cholesterol^{16 17 18} which tends to maintain a constant level of cholesterol in the plasma.

The fact that dietary cholesterol does not influence arteriosclerosis was emphasized by Halden and Prokop¹⁵ about 20 years ago; recently, Oliver¹⁹ has summarized present thought in these words: "The evidence incriminating dietary cholesterol as a cause of coronary heart disease in developed countries is virtually non-existent."

Under normal circumstances, tissues cholesterol forms an integral part of cell membranes; it forms part of the various lipoproteins in plasma and is a precursor of bile acids. About 2 percent is used in the synthesis of adrenal and sex hormones.

In a wide variety of pathological conditions, cholesterol forms a large part of the lesion. This is true in scars, tubercles, gummata, old

⁹ Dock, W. J. *Am. Med. Assn.* 131 : 875, 1946.

¹⁰ Noble, N. L., R. J. Boucer and K.Y.T. Kao *Circulation* 15 : 366, 1957.

¹¹ Barr, D. P., E. M. Russ and H. D. Eder *Am. J. Med.* 11 : 480, 1951.

¹² Rhoads, G. G., C. L. Gulbrandsen and A. Kagan *New Eng. J. Med.* 294 : 293, 1976.

¹³ Leupold, E. and L. Bogendörfer *Deutsch. Arch. Klin. Med.* 140 : 28, 1922.

¹⁴ Tunidiff, R. J. *Infect. Dis.* 33 : 285, 1923.

¹⁵ Halden, W. and L. Prokop "Cholestrin, Ernährung, Gesundheit" Urban and Schwarzenberg, Vienna, 1957.

¹⁶ Gould, R. G. *Am. J. Med.* 11 : 209, 1951.

¹⁷ Tomkins, G. M., H. Sheppard and I. L. Chaikoff *J. Biol. Chem.* 201 : 137, 1953.

¹⁸ Siperstein, M. D. *Curr. Top. Cell Regul.* 2 : 65, 1970.

¹⁹ Oliver, M. *Brit. Heart J.* 38 : 214, 1976.

fibroids, thrombi, cholesteatomata; it occurs in combination with calcium, fibrin, collagen, and other substances.

The gradual accumulation of cholesterol in pathological lesions has been particularly well described for so-called *granulomatous lesions*. Hadfield²⁰ defines such lesions as a convenient term for the immature and highly fertile mesenchyma which invades and subsequently replaces dying or ill-nourished tissues in a number of pathological conditions. The center of such a lesion is composed of cholesterol, calcium, collagen, fibrin, etc., all of which serve to isolate the initiating agent of the disease, for instance, the tubercle bacillus, the spirochaete of syphilis, etc. Cholesterol may be thought of as a material which walls off the initiating agent. Moreover, one cannot ignore the previously mentioned possibility, that, in some other way, it aids resistance to disease. The initial response to an agent may be rather specific, but the advanced lesion may resemble many others histologically,²¹ and the final granuloma can be viewed as a compromise between ongoing repair processes and the continued assault of the initiating agent.

The developing atheroma has many of the features of a specific granulomatous lesion. The intima is invaded by modified smooth muscle cells,^{22, 23} and these early lesions do not contain any more lipid than the surrounding tissue.¹⁰ Gradually, the characteristic plaque develops, made up of the modified smooth muscle cells, collagen, debris from dying cells, and varying amounts of lipid including crystals of cholesterol. (The possible role of cholesterol as a "filler" in arteriosclerosis was pointed out by Halden and Prokop twenty years ago).¹⁵ It is inviting to speculate that the arteriosclerotic lesion is a specific granuloma and that cholesterol is present as a consequence of the lesion and not as its cause. This idea probably goes back to Virchow and was clearly mentioned by Leary.²⁴

We can now try to interpret some of the facts about cholesterol in light of a hypothesis that cholesterol is part of a repair process.

Its gradual accumulation in the arteriosclerotic lesion can be seen as a protective mechanism. The undoubted correlation of high serum cholesterol levels with a higher incidence of myocardial infarcts and strokes does not permit one to draw any conclusions as to which is the primary event, the lesion or the elevated serum cholesterol and whether there is a causal relationship at all. An elevated serum cholesterol may be viewed as a response to increased need of cholesterol for the formation of the granuloma.

Many investigators consider that elevated serum levels of the low density lipoproteins (Fredrickson Type II classification),²⁵ which carry approximately 70 percent of the serum cholesterol, are implicated in the development of arteriosclerotic lesions. This is based on the high cholesterol content of this fraction and on the fact that individuals with genetically abnormally high levels of this lipoprotein fraction have widespread arterial lesions and a higher incidence and an earlier onset of myocardial infarctions.

²⁰ Hadfield, G. *Ann. Roy. Coll. Surgery, Eng.* 9: 397, 1951.

²¹ Des Prez, R. in *Cecil-Loeb Textbook of Medicine*, 13th Ed., P. B. Beeson and W. McDermott, Eds. W. B. Saunders, Philadelphia, 1971.

²² Koss, R. and J. A. Glomset *Science* 180: 1332, 1973.

²³ Benditt, E. P. *Scient. Amer.* 236: 74, 1977.

²⁴ Leary, T. *Arch. Path.* 17: 453, 1934.

²⁵ Fredrickson, D.S., R. I. Levy and R. S. Lees *New Eng. J. Med.* 276: 273, 1967.

However, it has been pointed out^{26, 27} that the natural history of this disease differs completely from that of arteriosclerosis. Familial hypercholesterolemia is associated with lipid deposits in the arteries of nearly all organs and is probably more related to the cholesterol storage disease seen in animals fed large amounts of cholesterol. Furthermore, in contrast to arteriosclerosis, the fatty lesions involve the muscular layer of the arteries.^{26, 27} Fredrickson and Levy discuss the possibility that the initial vascular damage may be brought about by factors other than elevated LDL levels.²⁸ Fredrickson emphasizes that reduction of hyperlipidemia has not led to any measurable beneficial effect.⁸

The possible relationship of hyperlipoproteinemias to arteriosclerotic lesions has attracted the attention of many investigators. Of special interest are the findings of Brown and Goldstein²⁹ and of Miller and Miller and Glomset,^{30, 31} despite the fact that they interpret their observations in terms of the prevailing lipid theory of arteriosclerosis.

Brown and Goldstein have described what appear to be receptors for low density lipoproteins in fibroblasts. They believe that interaction of LDL with these receptors is the first step in the degradation of these lipoproteins and release of cholesterol, which serves to switch off synthesis of cholesterol in the cell. They found that the number of these receptors is reduced in familial hypercholesterolemia and, therefore, LDL accumulates in the serum. Now, according to the authors, cholesterol can exert its "lethal" effect; they imply that changes of this sort may play a part in the etiology of arteriosclerosis.

It is by no means sure whether the disseminated arterial disease can be ascribed to a primary defect in LDL receptors or whether there is a still more basic tissue lesion. However, the important point is that familial hypercholesterolemia can in no way be equated with arteriosclerosis. Even if LDL receptors are reduced in arteriosclerosis, this does not tell us anything about the initial lesion and should not allow a value judgment as to the ensuing lipid changes.

About 25 years ago, it was noted that the serum high density lipoprotein fraction is reduced in arteriosclerosis.¹⁰ More recently,^{12, 30, 31} evidence has been presented that the HDL fraction transports cholesterol from the tissues to the liver for catabolism and excretion. Lower levels of HDL have been found with high tissue cholesterol levels and in hypercholesterolemia, hypertriglyceridemia, obesity, diabetes mellitus, patients with ischaemic heart disease, and in males in general. Under the influence of the lipid theory, it is hypothesized that this defect in cholesterol transport is an etiological factor in arteriosclerosis whereas it may, in fact be a consequence of the disease. In the same way, high HDL levels seen in long-lived individuals may be a reflection of their longevity rather than the cause—if there is any causal relationship at all.

²⁶ Wolman, M. in "Handbuch der Histochemie," vol. 5/2 W. Grauman and R. Neumann, Eds. Gustav Fisher Verlag, Stuttgart, 1964, p. 239.

²⁷ Watanabe, T., K. Tanaka and N. Yanai *Acta Path. Jap.* 18 : 319, 1968.

²⁸ Fredrickson, D. S. and R. I. Levy in "The Metabolic Basis of Inherited Disease," 3rd Ed. J. B. Stanbury, J. B. Wyngaarden and D. S. Fredrickson, Eds. McGraw Hill, New York, 1972, p. 545.

²⁹ Brown, M. S. and J. L. Goldstein *Science* 191 : 150, 1976.

³⁰ Miller, G. J. and N. E. Miller. *Lancet* I : 16, 1975.

³¹ Glomset, J. A., *J. Lip. Res.* 9 : 155, 1968.

The exacerbation of arteriosclerotic lesions in nephrosis, which is associated with high serum cholesterol levels, is not necessarily a consequence of the elevated cholesterol. Nephrosis is a generalized disease which may affect and enhance any existing lesions, including those of arteriosclerosis. Cholesterol disposition may well be a consequence of the exacerbation of the arteriosclerotic lesions by the basic disease.

Arterial degenerative lesions have been studied in free-ranging animals and in laboratory animals fed so-called "atherogenic" diets. In free-ranging animals, no lesions have been found that are comparable to those observed in man. When diets are fed which contain large amounts of cholesterol and so much saturated fat as to be deficient in essential fatty acids, some species (especially rabbits and chickens) develop arterial deposits of cholesterol. Most species are resistant to this cholesterol deposition, even under these conditions. In the absence of a so-called "atherogenic diet," the chicken does spontaneously develop an arterial lesion which resembles the human lesion in its inception as opposed to the lesion which develops after feeding of cholesterol.²⁴ When rabbits and chickens are flooded with cholesterol, deposits occur in the arteries of many organs which are perhaps comparable to those occurring in familial hypercholesterolemia but different from the plaques found in human arteriosclerosis.

The histological resemblance between degenerative lesions in swine and man has promoted use of this animal in experimental models of the disease.³² However, differences in the natural history of the disease in swine and human arteriosclerosis are too great to justify comparisons. Arteries, after all, have only a limited response potential.³³

Considerable effort has gone into demonstrating the presence of arteriosclerotic lesions in nonhuman primates. In those living in the wild, sudanophilic changes in the aorta have been reported,^{34, 35} but the incidence varies widely from species to species.³⁶ Even in squirrel monkeys, which have the most lesions, the lesions are considerably less severe than in human populations with the least arteriosclerotic involvement. The appearance of these lesions differs markedly from human lesions in being hardly visible to the naked eye; furthermore, there are no obstructive coronary episodes.³⁷ In captivity, if they are fed unphysiological diets (containing cholesterol and butter), more severe lesions are seen, but, here too, the natural history of their disease is completely different from the human disease. Thus, the degenerative disease of the arteries of subhuman primates is only superficially similar to the human disease and may be caused by entirely different factors.

The difficulties in interpreting findings on primates are exemplified in an article by Ross and Harker³⁸ describing studies with pig tail monkeys. The authors discuss the effect of platelets on muscle cells of the arteries. Injuries to such cells led to their proliferation under the impact of a platelet factor (or factors). However, the report deals

³² Luginbuhl, H. and J. E. T. Jones in "Comparative Atherosclerosis," J. C. Roberts and R. Straus, Eds. Harper & Row, New York, 1965, p. 3.

³³ Blumenthal, H. T. in "Cowdry's Arteriosclerosis," H. T. Blumenthal, Ed. Charles Thomas, Springfield, 1967, p. 83.

³⁴ McGill, H. C., Jr., J. P. Strong, R. L. Holman and N. T. Werthessen *Circ. Res.* 8: 670, 1960.

³⁵ Gresham, G. A. and A. N. Howard *Ann. N.Y. Acad. Sci.* 127: 694, 1969.

³⁶ Eggen, D. A., J. P. Strong and W. P. Newman III. *Ann. N.Y. Acad. Sci.* 162: 110, 1969.

³⁷ Strong, J. P. and N. C. Tappen. *Arch. Path.* 79: 199, 1965.

³⁸ Ross, R. and L. Harker. *Science* 193: 1094, 1976.

mainly with effects of hyperlipidemia, which they think may produce the original lesion leading to the formation of an atheroma (by implication, not only in the pig tail monkey but also in man). This conclusion was reached in studies in which pig tail monkeys weighing 1.5 to 3.0 kg were fed a formula diet affording a daily intake of at least 20 grams of powdered egg yolk and 12 grams of corn oil in addition to any lipid in their monkey chow. In human terms, this would amount to perhaps 700 grams of powdered egg yolk and 400 grams of corn oil. Such a diet would induce a variety of metabolic changes in the whole organism. It is difficult to understand why just the hypercholesterolemia is singled out as an important factor. Such a regimen could well induce lipid deposits in most organs comparable to those seen in cholesterol-fed rabbits and in humans with familial hypercholesterolemia and in contrast to what occurs in human arteriosclerosis. Unfortunately, this report does not mention any organs other than some of the arteries. It is interesting, nevertheless, that these authors finally conclude that injury to the arteries may set off "a process which probably is an attempt at healing the injury but which can lead to atherosclerosis".³⁹

All of this leads me to conclude that no animal models have been found which are sufficiently similar to human arteriosclerosis to permit etiological conclusions. So far, it seems that arteriosclerosis is a specific human disease. A similar conclusion was reached by Duff and McMillan some twenty-five years ago.⁴⁰

At this point, it may be well to discuss briefly how thinking about cholesterol has been influenced by statistical studies of the incidence of various degenerative diseases. The concept of "risk factors" has risen from the undeniable evidence that people with hypertension, obesity, addiction to heavy smoking, or high serum cholesterol levels have, as a group, a higher incidence of arteriosclerotic disease. Denoting all of these factors as "risk factors" suggests that they have the same relationship to the disease. It may well be that excessive smoking or obesity is a causative factor in the disease, whereas elevated serum cholesterol levels are a consequence of the disease. Reports of the Framingham study have been guilty of this error in not paying heed to the fact that statistical associations cannot be construed as causal relationships, and this has impeded progress in this field.

If this difficulty were only of semantic interest, it would not be so important. However, insistence on cholesterol as a causative agent has led to all sorts of attempts to lower serum cholesterol, some of which have been harmful (Triparanol, for example, or estrogens). More recently, the National Heart and Lung Institute reported that, on the basis of findings in the Coronary Drug Project, such hypocholesterolemic drugs as clofibrate and niacin have no influence on the survivors of myocardial infarctions.⁴¹

The fact that the intake of butter is associated with higher serum cholesterol values and that feeding of corn oil leads to lower levels has been established beyond any doubt.^{42, 43} In contrast, there is any-

³⁹ Kaunitz, H. J. *Am. Oil Chemists Soc.* 52: 293, 1975.

⁴⁰ Duff, G. L. and G. C. McMillan. *Am. J. Med.* 11: 92, 1951.

⁴¹ Coronary Drug Project Research Group. *J. Am. Med. Assn.* 226: 652, 1973.

⁴² Ahrens, E. H., Jr., W. Insull, Jr., R. Blomstrand, J. H. Hirsch, T. T. Tsaltas and M. L. Peterson. *Lancet* I: 943, 1957.

⁴³ Beveridge, J. M. R., W. F. Connell, G. A. Mayer and H. L. Haus. *Can. J. Biochem.* 36: 895, 1958.

thing but unanimity about whether the hypercholesterolemic effect of some of the vegetable oils is the result of sterol or bile acid excretion. A number of examiners have reported that the serum-cholesterol-lowering effect of unsaturated oils is associated with increased excretion of sterols and bile acids.^{44, 45, 46} Others are of an entirely different opinion. Gran and Nicolaysen⁴⁷ thought that there is a redistribution of cholesterol in the body pools rather than increased excretion, and Grundy and Ahrens^{48, 49} were of the same opinion after careful studies in humans fed different fats. This latter idea is compatible with the finding by Gerson et al.⁵⁰ of an increase in the level of cholesterol in many organs (including arteries) after intake of unsaturated fat.

One can not help but have the impression that so much effort has been invested in such studies because it has been taken for granted that cholesterol is an atherogenic substance and that its overall reduction in the body could only be an advantage for the individual.

A subject of heated discussion is the possibility of tissue damage brought about by the excessive intake of polyunsaturated fatty acids. Especially in the U.S., many workers, Tappel and Mead among them,^{51, 52} believe that the intake of linoleate results in increased free radical formation and tissue peroxidation, which in turn can bring about destruction of cell membranes, especially in the absence of sufficient vitamin E. Such tissues often show abnormal (ceroid) pigmentation, which is thought to be due to the formation of fat polymers. A group of English workers⁵³ admit the possibly destructive effect of polyunsaturated fatty acids and emphasize the importance of tocopherol but do not believe in the existence of tissue peroxides. However, Mukai and Goldstein have presented some evidence that malonaldehyde, a derivative of linoleic acid brings about abnormal crosslinking of DNA in bacteria to produce increased mutagenesis.⁵⁴ They are attempting to obtain evidence that alterations in DNA in human erythrocytes may perhaps occur even in the presence of vitamin E.⁵⁵

In any discussion of the nutritional effects of animal vs vegetable fats, one should not ignore the fact that fatty acid composition and degree of unsaturation are only two properties of fats. Fats and oils contain from 2-4 percent of nontriglyceride material. Vegetable oils may contain a wide variety of active materials which vary from fat to fat. Butter contains a number of substances responsible for its characteristic aroma, but does not contain as many compounds as most vegetable oils.

Although studies of the pharmacological effects of nontriglyceride substances are few, it has been reported that the elevation of serum

⁴⁴ Malmros, H. *Lancet* II: 479, 1969.

⁴⁵ Connor, W. E., D. T. Witiak, D. B. Stone and M. L. Armstrong. *J. Clin. Invest.* 48: 1363, 1969.

⁴⁶ Nestel, P. J., N. Havenstein, H. M. Whyte, D. P. Trevor, J. Scott and L. J. Cook. *New Eng. J. Med.* 288: 379, 1973.

⁴⁷ Gran, F. C. and R. Nicolaysen. *Acta Phys. Scand.* 68: 169, 1966.

⁴⁸ Grundy, S. M. and E. H. Ahrens, Jr. *J. Clin. Invest.* 49: 1135, 1970.

⁴⁹ Grundy, S. M. and E. H. Ahrens, Jr. *J. Lip. Res.* 10: 91, 1969.

⁵⁰ Gerson, T., F. B. Shoreland and Y. Adams. *Biochem. J.* 81: 584, 1961.

⁵¹ Tappel, A. in "Pathological Aspects of Cell Membranes" Academic Press, New York, 1971.

⁵² Mead, J. F. *Am. Chem. Soc. Feb.* 1972: 70.

⁵³ Green, J., A. T. Diplock, J. Bunyan, D. McHale and F. R. Muthy. *Brit. J. Nutr.* 21: 69, 1971.

⁵⁴ Murai, F. H. and B. D. Goldstein. *Science* 191: 868, 1976.

⁵⁵ Goldstein, B. D. and E. M. McDonagh. *Clin. Res.* 23: 274A, 1975.

cholesterol after intake of milk fat can be induced by feeding its nontriglyceride fraction.⁵⁶ Moreover, it has been reported that the serum cholesterol-lowering effect of corn oil persists after hydrogenation of the oil,⁵⁷ which suggests that the effect may not be due to its linoleic acid content but to compounds in the nontriglyceride fraction.

In a long-term study carried out in our laboratory,⁵⁸ we fed groups of 40 weanling male rats diets containing 20 percent of one of ten fats and observed them throughout their lifespan. The rats died with a variety of infections, neoplastic and degenerative diseases. Most rats were found to have varying degrees of cardiac fibrosis, and statistical evaluation of the results of histological examinations of heart sections showed that the groups fed olive oil and the linoleate rich cottonseed, soybean, and corn oils had more severe cardiac fibrosis ($P < .01$) than did those fed lard, beef fat, chicken fat and milk fat. Many of the rats had marked proliferation of the bile ducts, and here, too, the changes were more pronounced in the rats fed vegetable oils. In the same study, there were significant ($P < .02$) differences in tumor incidence, with the group fed milk fat having the lowest incidence.

In a long-term experiment in which rats and mice were fed butterfat, coconut oil, or soybean oils with various degrees of hydrogenation at a level of 60 percent of calories, it was concluded that there were no differences in survival rate and pathological changes that could be related to the kind of fat fed.⁵⁹ In studies in which Getty observed the occurrence of widespread degenerative, arterial lesions in old swine, he remarked that those animals consumed mainly unsaturated vegetable oils as their dietary fat.⁶⁰

Literature dealing with the role of dietary fat in human arteriosclerosis and its complications is extensive and confusing. It has been claimed repeatedly that there is a positive correlation between fat intake and the occurrence of severe arteriosclerotic lesions and of myocardial infarctions. However, more recently, questions have been raised as to the validity of this association, especially by Klevay.⁶¹ A great deal of work has been invested in trying to establish whether or not the intake of unsaturated fats is advantageous in preventing or treating arteriosclerosis. Unfortunately, objections can be raised against essentially all studies because of poor methodology. Even if blind studies were carried out, which was relatively rarely, caloric intakes and body weights are not reported or, if they are, there frequently are differences between experimental and control groups. Inasmuch as caloric intake and body weight are correlated with the incidence of coronary heart disease,^{62 63 64} attention should be paid to these parameters in studies purporting to compare specific dietary fats.

⁵⁶ Beveridge, J. M. R., W. F. Connell and G. A. Mayer. *Can. J. Biochem.* 35: 257, 1957.

⁵⁷ Malmros, H. in "Essential Fatty Acids," H. Sinclair, Ed. Academic Press, New York, 1958.

⁵⁸ Kaunitz, H. and R. E. Johnson. *Lipids* 8: 329, 1973.

⁵⁹ Vles, R. O. and J. J. Gottenbos. *Voeding* 33: 428, 1972.

⁶⁰ Getty, R. in "Comparative Atherosclerosis," J. C. Roberts and R. Strauss, Eds. Harper & Row, New York, 1965, p. 11.

⁶¹ Klevay, L. M. *Am. J. Clin. Nutr.* 27: 1202, 1974.

⁶² Assn. Life Ins. Med. Dir. and Act. Soc. of America "Medico-actuarial Mortality Investigation," vol. I. New York, 1912.

⁶³ Society of Actuaries "Build and Blood Pressure Study," vol. I. Chicago, 1959.

⁶⁴ Dublin, L. I. and H. H. Marks. Mortality among insured overweighters in recent years. Read at 60th Annual Meeting of the Assn. Life Ins. Med. Dir. of America, October 1951, New York.

The importance of such considerations is illustrated in studies by Bierenbaum et al.^{65 66} in which patients receiving diets containing 28 percent of calories as fats with unsaturated to saturated ratios of 3:1 and 1:3 were compared with an uncontrolled group. Both controlled groups, regardless of the degree of unsaturation of their diet, had lower serum cholesterol, lower body weights, and a lower incidence of myocardial infarction. In this study, it is not possible to separate the effects of weight and cholesterol as etiological factors.

Groen et al.⁶⁷ studied comparable groups of Trappist and Benedictine monks, the former living on a vegetarian diet and the latter, on a mixed Western diet. The average serum cholesterol was significantly higher among the Benedictine monks, but there was no difference in the incidence of myocardial infarction, angina pectoris, hypertension, or signs of ischemic heart disease.

In one Norwegian study lasting five years,⁶⁸ persons eating soybean oil had lower serum cholesterol levels and fewer heart attacks than did the control group having the typical fat intake of Norway. However, the control group consumed about 3000 calories/day whereas the group fed soybean oil ate 2400 calories, lost an average of 4 to 5 pounds, and maintained this reduced weight. It is by no means convincing that the somewhat reduced incidence of myocardial infarction in the diet-controlled group was due to their lower serum cholesterol levels. The same groups were followed for a second 5-year period without supervision or dietary advice.⁶⁹ By the end of this followup period, there had been a significantly lower overall incidence of fatal myocardial infarction in the group which had been the original diet-controlled group. However, there are no data as to adherence to dietary regimen, changes in body weight and serum cholesterol levels, and blood pressures for the followup period.

In a similar study carried out in London, the addition of 85 grams of soybean oil in exchange for saturated fat did not change the clinical course of their disease in 199 men who had sustained myocardial infarctions compared to the controls on a freely selected diet.⁷⁰

In a twelve-year study carried out simultaneously in two Finnish mental hospitals,⁷¹ the patients were given the experimental polyunsaturated diet and those in the other hospital served as controls with their usual diet; of necessity, this was not a blind study. After six years, the dietary regimens were reversed and the study continued for another six years. It is reported that, among male patients, there was a significantly ($P < .002$; $P < .06$) reduced mortality from coronary heart disease while the groups were given soybean oil and a small, but not statistically significant, decrease in overall mortality. Among female patients, there was no effect on overall mortality. The authors emphasize the difficulty in assessing fluctuating populations and in

⁶⁵ Bierenbaum, M. L., D. P. Green, A. Florin, A. I. Fleischman and A. B. Caldwell. *J. Am. Med. Assn.* 202: 1119, 1967.

⁶⁶ Bierenbaum, M. L., A. I. Fleischman, R. I. Raichelson, T. Hayton and P. B. Watson. *Lancet* I: 1404, 1973.

⁶⁷ Groen, J. T., K. B. Tioong, M. Koster, A. F. Willenbrands, G. Verondick and M. Piercoot. *Am. J. Clin. Nutr.* 10: 456, 1962.

⁶⁸ Ieren, P. *Acta Med. Scand. Suppl.* 466: 196, 1966.

⁶⁹ Ieren, P. *Circulation* 48: 935, 1970.

⁷⁰ Report of a Research Committee to the Medical Research Council, J. N. Morris, Chairman of the Committee. *Lancet* II: 693, 1968.

⁷¹ Miettinen, M., O. Turpeinen, M. J. Karvong, R. Elosuo, and E. Paavilainen. *Lancet* LL: 7782, 1972.

comparing psychiatric patients with a normal population. However, the most important flaw was the absence of data on food intake and body weight.

In a double blind study carried out in California over a period of nine years,⁷² two groups were fed animal and vegetable fats. Death rates were identical in the two groups. If all arteriosclerotic events were combined, the incidence was somewhat lower in the vegetable oil group. Chemical analyses of aortic material taken at autopsy revealed no differences in the concentrations of various lipid fractions between the two groups. In view of the fact that the mortality rate was the same in the two groups, one can not help but think that differences in dietary fat were not important, especially in view of the fact that data as to weight and food intake were not given and adherence to the diet was not ideal.

Clinical studies involving butter were carried out at the Bundesanstalt für MilCHForschung in Kiel.⁷³ Butter with a linoleate content of 5 percent was compared with a margarine containing 12.5 percent of linoleate. About 1,000 patients were kept on the experimental diet for from one to five years and were examined for many parameters. Serum cholesterol values were higher in the butter group after 4-6 weeks but were lower after one year. Total serum lipids and triglycerides were higher in the group fed margarine. Examinations of eye grounds, electrocardiograms, and blood pressures revealed no differences in the groups.

Some results are completely at variance with the "lipid theory". In one study,⁷⁴ patients who had previously had myocardial infarctions were given a diet high in polyunsaturated fats and low in cholesterol. Mortality was lower in this group than among the controls on a conventional diet although the controls had lower serum cholesterol levels than those given polyunsaturated fat.

In another study,⁷⁵ it was concluded that corn oil can not be recommended as a treatment of ischaemic heart disease because of a high incidence of re-infarction in the patients provided with corn oil. However, the small number of subjects and the way of administering corn oil make it difficult to accept the authors' conclusion without reservation.

Two studies carried out by the British Medical Research Council in patients with previous myocardial infarction showed a low-cholesterol, polyunsaturated fat diet was not particularly beneficial.^{76, 77}

Malhotra studied paired railroad workers from two parts of India in which the risk of coronary disease differed by a factor of 15. Workers from the area of lower risk ate more fat with a higher degree of saturation than did those from the area of higher risk. The serum cholesterol levels were almost identical in the two groups.⁷⁸

There are a number of other reports dealing with the relationship of dietary fat to the etiology of coronary heart disease, including some

⁷² Dayton, S., M. L. Pearce, S. Hashimoto, W. J. Dixon and O. Tomiyasu. *Circulation* 40, suppl. 11: 196, 1969.

⁷³ Lemke, A., H. Frahm, H. Gregersen, U. Lembke and E. Weber. *Kiel. Milchwirt, Forschungsber.* 24: 3, 1972.

⁷⁴ Hood, B., H. Sanne, G. Örndahl, M. Ahlström and G. Welin *Acta Med. Scand.* 178: 161, 1965.

⁷⁵ Rose, G. A., W. B. Thomson and R. T. Williams. *Brit. Med. J.* 1: 1531, 1965.

⁷⁶ Medical Research Council. *Lancet* II: 501, 1965.

⁷⁷ Medical Research Council. *Lancet* II: 693, 1968.

⁷⁸ Malhotra, S. L. *Am. J. Clin. Nutr.* 20: 462, 1967.

from anticoronary clubs, but they are of dubious value because of their lack of scientific methodology.

In an exhaustive survey of the literature dealing with coronary heart disease, especially in relation to diet, a committee of the Royal Society of New Zealand concluded that "so far as the general population is concerned the present stage of knowledge does not justify advising any major changes in dietary habits aimed specifically at reducing the incidence of CHD"⁷⁹. Ahrens has recently expressed the same opinion.⁸⁰

Diet certainly does play a part in the development of arteriosclerosis, as it does in many diseases. However, this may represent only its effect on body weight. Many dietary constituents other than lipid (saccharose, minerals, fiber, protein) have been proposed as etiological factors, but there is as yet no clearcut evidence that any specific dietary factors adversely affect the condition unless they are present in unphysiological amounts (too much or too little). A similar view has recently been expressed by Burch.⁸¹

With regard to the initial lesion which gives rise to the arteriosclerotic lesion, two theories receive most attention. One considers that the initiating factor may be mechanical injury to the arterial wall which eventually results in an atheroma. Animal experiments carried out to mimic such an injury are of dubious value because it is unlikely that animals harbor a disease comparable to human arteriosclerosis. Moreover, Benditt has pointed out that the cells present in the atheroma are biologically different from those appearing as a reaction to an injury of the arterial wall.²⁴

Considerably more evidence seems to accumulate in favor of an infectious etiology. More than one hundred years ago, Virchow thought that the arteriosclerotic lesion is initiated by various bacterial and other toxins.⁸² At the present time, Burch has proposed that "viral infections in early life could be one of the most important initiating causes of vascular lesions which develop into arteriosclerotic lesions."⁸¹ He has enumerated a number of viruses which he thinks could initiate the process.

As corollary to these thoughts, we may cite the appearance of extra- and intracellular cholesterol crystals in cells infected with feline herpes virus.⁸³

Studies by Benditt and Benditt⁸⁴ suggest that mutagenic factors, possibly viral or chemical, bring about a proliferation of modified smooth muscle cells, which Benditt believes may be tumor-like in nature.

However, the possibility that we are dealing with a specific infectious disease should not be eliminated.⁸⁵ The epidemic-like outbreak of myocardial infarction and strokes during the last 50 years points in this direction. One may think of the discovery of slow viruses.⁸⁶ Also,

⁷⁹ Committee of the Royal Society of New Zealand, "Coronary Heart Disease," Wellington, New Zealand, p. 79.

⁸⁰ Ahrens, E. H., Jr. *Ann. Int. Med.* 85 : 87, 1976.

⁸¹ Burch, G. E. *Am. Heart J.* 87 : 407, 1974.

⁸² Virchow, R. in "Gesammelte Abhandlungen zur wissenschaftlichen Medizin" Meidinger, Frankfurt, 1856.

⁸³ Fabricant, G. G., L. Krook and J. H. Gillespie. *Science* 181 : 566, 1973.

⁸⁴ Benditt, E. P. and J. M. Benditt, *Proc. Nat. Acad. Sci.* 70 : 1753, 1973.

⁸⁵ Gajdusek, D. C. *Adv. Geront. Res.* 4 : 201, 1972.

⁸⁶ Marx, J. L. *Science* 196 : 151, 1977.

the fact that the arteriosclerotic lesion resembles a specific granuloma invites speculation about a specific agent. I hesitate to call it a virus because the history of the conquests of the major chronic diseases shows that entirely new classes of organisms were found for each one. Thus, an entirely new microorganism provoking unknown immune responses may be responsible for human arteriosclerosis.

It must be clear that any discussion as to the initiating factor in arteriosclerosis is based on rank speculation. However, the idea that dietary factors per se can be initiating factors should be abandoned. This idea has prevented progress in this field in our century.

UNIVERSITY OF ILLINOIS,
Urbana-Champaign, Ill., May 12, 1977.

Senator GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you for your letter of May 2, 1977, a copy of Dietary Goals for the United States and a copy of Senate Bill 1420, a bill to amend the National School Lunch Act. I am concerned about the information to be "taught" as nutrition. Will the teachers recommend that children not eat eggs to avoid cholesterol? The Agricultural Extension Service already has a nutrition program and has had one for a number of years. Yet, soft drink consumption has increased as shown in your report.

It is stated in the report on page 78 "There is insufficient knowledge about food habits, choice and motivations." I suggest the Senate Select Committee on Nutrition and Human Needs ask representatives of the advertising agencies involved in the expenditure of \$1,159,522,600 for food and beverage ads about motivation (page 62). They have studied motivation extensively and can provide answers on this subject.

I am enclosing my reprints on the role of fat in the diet, a reprint of a joint paper with Dr. Gotto's group and a galley proof of a paper which will appear in the May issue of the American Journal of Clinical Nutrition. I fully agree with Drs. Levy, Gotto and Stamler that Americans eat too much fat and sugar, but I cannot agree with the recommendation to eliminate eggs or sources of animal fat from the diet. Your data indicates that animal fat consumption has decreased 24 pounds and vegetable fat consumption has increased 34 pounds/capita from 1940 to 1974. Yet, coronary heart disease has increased during a time period that this change took place. Why blame animal fats? I just came back from a National Academy of Sciences Visitor Exchange in Romania. I saw people in Bucharest lined up at butcher shops for meat, but not other shops, which indicates to me that they would like to eat more meat than they do.

Decreasing meat consumption by 65 pounds/capita in the USA, or equivalent to the consumption in Romania, may cause similar shortages at our supermarkets. A large surplus may at first develop, but in a free economy so many cattle and hog farmers will go out of business that shortages may well develop. I doubt if many American consumers would be happy standing in line as readily as the disciplined people in Bucharest.

I'll be glad to provide you a write up of my views for your records. However, I believe you ought to reopen the hearings and look at all sides of this question before your committee recommends that children stop drinking whole milk and stop eating eggs.

Sincerely yours,

F. A. KUMMEROW,
Director, The Burnsidess Research Laboratory.

Enclosure.

UNIVERSITY OF ILLINOIS,
Urbana-Champaign, Ill., May 12, 1977.

DR. AUREL MOGA,
President, Academy of Medical Sciences of the Socialist Republic of Romania, Bucharest, Romania.

DEAR DR. MOGA: Please find enclosed a copy of my report to the National Academy of Sciences in regard to my visit to Romania and a copy of a brochure entitled "Collaboration in Cardiovascular Research" between the NIH and the Union of Soviet Socialist Republics. I hope that the Romanian National Council for Science and Technology will allow a similar cooperative effort. Because of the diversity of dietary habits and food availability, Romania could provide invaluable data on the possible relationship between diet and heart disease. I noted from my one month of observation in various parts of Romania that a rapid increase in the incidence of heart disease is taking place in the urban, but not the rural areas, in Romania. You are in a position of eminence to call attention to this trend.

After my return to Urbana, I summarized some of the data provided by Drs. Pitea and Ohra and compared it to the latest information I could find in the USA (Table II). I'm checking with Dr. Pitea and Dr. Ohra to make sure the data for Romania are correct. I believe that bread is a main source of protein and carbohydrate in Romania. Sugar consumption is almost as high as in the USA, however, very little hydrogenated fat is available in Romania. A collaborative study on lumberjacks in Tirgus Mures could be carried out with Dr. Nikkila and Dr. Miettinen in Helsinki. I spent ten days in October, 1973 in Helsinki and visited the Unilever Brothers plant there with Dr. Miettinen. Your food shops do not contain the same type of fats as I noted in Helsinki or Western Europe. There is an effort to reduce meat consumption in the USA, although only 65 pounds/capita less meat is consumed in Romania than in the USA. I saw people standing in line in Bucharest at the butcher shops, which indicates to me that Romanians would like to eat more meat than they do.

I suggest that you consider creating three research centers to cooperate with the National Heart, Lung and Blood Institute. One at Cluj with Dr. T. A. Popescu as director, one at Tirgus Mures with Dr. A. Horvath as director and one at Bucharest with Dr. I. Ohra as director. Drs. Popescu and Horvath could study subjects in the rural areas and compare their results with Dr. Ohra in Bucharest. This would not require elaborate funding as the hospitals and laboratory staff are already available in all three areas. Dr. I. Mincu is primarily interested in diabetes rather than heart disease; however, his laboratory could serve as an added laboratory in Bucharest.

If I can do anything to help, please let me know.

Sincerely yours,

F. A. KUMMEROW,
Director, The Burnsidess Research Laboratory.

To: The National Academy of Sciences, 2101 Constitution Avenue, Washington, D.C. 20418.

From: F. A. Kummerow, The Burnsidess Research Laboratory, University of Illinois, Urbana, Illinois 61801.

Subject: Report on my Exchange Visit with the Romanian Academy of Sciences.

This report is divided into three sections: (1) a summary, (2) a detailed report by F. A. Kummerow in regard to visits at the three research oriented medical schools in Romania, and (3) a report by Amy L. Kummerow in regard to primary and secondary education in Cluj and Bucharest. Summary:

First, my wife and I would like to thank the Romanian Academy of Sciences for a friendly, pleasant and informative visit. We were treated most courteously by everyone we came in contact with. Maybe sharing the tragedy of the earthquake drew us together into a common brotherhood and we were all able to feel a common sorrow that brought us closer together. We have visited Hungary and Bulgaria on a previous National Academy of Sciences Visitor Exchange Program and we have visited, during a six month sabbatical leave, the leading laboratories in both Western and Eastern Europe. We have always had warm, friendly receptions in every country we have visited probably because scientists have the same goals and aspiration regardless of the country of origin. We are particularly fond of the Romanians we met and we were impressed by the educational institutions from kindergarten to the university level.

The scientists I met during my visit in Romania are as competent as those in Western Europe or the USA. The system of medical care in Romania is somewhat analogous to Western Germany. I studied this system during a two month stay in Heidelberg in 1971 and I believe that the medical school at Cluj could be considered the Heidelberg of Eastern Europe. As the Krehl Clinic in Heidelberg houses all of the referral cases from Southern Germany, the First Department of Clinical Medicine at Cluj houses the referral cases from all of Northern Romania. Such a concentration of subjects with the same disease provides a rare opportunity for research and study at the postgraduate level. The research team of Drs. Popescu, Cucuianu, Berzu and Cuparencu that work together in Cluj are as competent and have a more basic research program than the internationally recognized team of Drs. Seidel, Gretten and Schlierf that work with Dr. Schettler at the Krehl Clinic. Dr. Schlierf had just returned from Washington, D.C. the day before our short visit with him in Heidelberg on our way to Bucharest. It is a tragedy for the recognition of Romanian medical research that the research team at Cluj does not have the same privilege of visiting with their peers in Western Europe and the USA.

Apparently, because of concern about defections, Romanian passport control does not allow freedom of travel for its researchers who, therefore, do not get stimulation or cross-fertilization of ideas and the recognition they deserve. It is unfortunate if someone does not return, for then it is even more difficult for others to get the opportunity to attend conferences and visit laboratories in other countries. I felt all those that I visited were intensely loyal to their country and wished to assist its progress. My main criticism would be that due to their

confinement within their country, Romanian scientists could not utilize and sometimes did not realize (particularly in Tirgus Mures where virtually no one had had outside contacts) the importance of their data and the value of further developing it to add to world-wide knowledge. Since January 1, 1977, Romanian medical researchers have been cut off almost completely from scientific journals published in Western Europe and the USA and they must sometimes wait for months for the simplest of chemical reagents. Yet, they keep on doing research. Romania is almost unique in its availability of clinical research subjects. Nowhere else in the world, even at Heidelberg, does a clinical researcher have such subjects to work with. That these subjects have not been considered a rare research privilege by Romanian researchers is due to their lack of knowledge of the clinical research situation in the USA and Western Europe. The Romanian Airline flies planes to Frankfurt and New York so hard currency is not necessary. If Romanian researchers were given a few more privileges and could compare their physical facilities with those in the West, there needn't be such a fear that they would not return to Romania.

What seems most unfortunate is that Russia, which seems to set the standards for its Eastern Satellites, has taken advantage of cooperation with the NIH on international research programs. I am enclosing with a copy of my report to Dr. Moga a brochure on this program. The National Science Foundation has had \$500,000/year of funds available to help Romanian science and because so few projects have been submitted, this fund has been reduced to \$167,000 for 1978. The NIH has tried for two years to develop cooperative research programs for Romanian medical researchers without success. On the other hand, Dr. Moga, President of the Medical Academy of Romania, told me during a two hour conversation with him in Bucharest that the Romanian government wants to be recognized for its medical achievements and it should be recognized because those achievements are considerable. However, how can such achievements be recognized if no one hears or reads about them? Furthermore, as I indicated in my detailed report, the Romanian medical community is capable of generating hundreds of millions of dollars through the development of new drugs for the treatment of heart disease. Clearly, somewhere in government management an understanding of how medical research could benefit Romania is lacking.

I am willing to help by writing a cooperative research proposal to the National Science Foundation on cell membranes, an area in which Dr. G. Benga of the Department of Biochemistry at Cluj could contribute to significantly. I also plan to explore with Dr. M. D. Leavitt, Director of the International Fogarty Program at the NIH, how I can help to develop cooperative NIH research proposals with qualified research workers at Romanian universities and medical schools. Dr. Cucuianu, in the paper he presented at the Ciba Foundation Symposium in 1973, stated "One of my favorite dreams is the creation of an International Research Center for Atherosclerosis and Thrombosis Research in Cluj." I believe that the implementation of this dream would bring international recognition to the Socialist Republic of Romania and would be of value to heart research because of the unique clinical material available and existing qualified staff.

DETAILED REPORT

By F. A. Kummerow

On our way to Bucharest, we had stopped in London for a visit with Dr. S. J. Darke, Department of Health, Dr. G. Schlierf of the Krehl Clinic in Heidelberg, and Dr. J. Valek of the Institute for Clinical and Experimental Medicine in Prague for the latest information on diet and heart disease in England, Germany and Czechoslovakia. Luckily, I stopped at the American Embassy in Prague in order to send a telex message that we would arrive in Bucharest on train number 373 and car number 54 from Prague on March 4, 1977. The train arrived two hours late; however, Dr. Ion Birliugu of the Romanian Academy of Sciences was on the train platform and recognized us before we had stepped out of the car. He had a taxi waiting and took us to the Dorobanti Hotel in downtown Bucharest. After checking into the hotel, he made financial arrangements with me and told us that he would meet me on Monday morning at 10:00 a.m. for the start of our visit. That plan never materialized.

At 9:24 p.m., the hotel started to vibrate and I immediately recognized an earthquake was responsible for the vibration. My wife and I ran down eight flights of stairs as fast as we could and were out of the hotel before the entire city was plunged in darkness. Power was restored shortly after 2:00 a.m. and we returned to our room at 3:00 a.m. The hotel was damaged, but it did not collapse. I stopped at the Romanian Academy of Sciences at 8:00 a.m. and made arrangements to see Dr. Gheorghe Ciucu, Secretary General, Academy of the Socialist Republic of Romania and then reported in at the American Embassy. The Embassy itself was damaged, but the staff was busily sending messages to the U.S.A. in regard to the safety of the Americans that continually came to the Embassy. We then returned to the Romanian Academy of Sciences and were taken to see Dr. Ciucu by a woman employee of the Academy. Dr. Ciucu told us that a visit to Cluj was planned for us and that Dr. Birliugu would get in touch with us on Monday at 10:00 a.m. as originally planned. We returned to the American Embassy in the afternoon and were told that the Intercontinental Hotel had been declared safe, but that they could not get any information on the safety of the Dorobanti Hotel. As more after-shocks were expected, and some as severe as 6 on the Richter scale did occur, we were advised to move to the Intercontinental Hotel, which we did. I paid 50 U.S. dollars for this room myself. Our room in the Intercontinental Hotel was even in worse shape than the room at the Dorobanti Hotel. The toilet paper holder in the bathroom had disappeared through a large hole in the wall and some of the tile had popped off the wall. We moved back to the Dorobanti Hotel Sunday evening and stayed there until Tuesday morning. It was largely deserted as a steady stream of guests had checked out as soon as they could get to their rooms and pack up their clothes.

Dr. Birliugu met us at 10:00 a.m. on Tuesday, March 8, and took us to the airport in an Academy car. He gave me additional funds at the airport for our hotel at Tirgus Mures and wished us a pleasant journey. After a 50-minute flight, we landed in Cluj; Dr. T. A. Popescu, Head of Clinical Cardiology at the Medical School in Cluj, was wait-

ing for us and drove us to the Napoca Hotel. We had lunch together and then Dr. Popescu took us on a tour of Cluj in his car.

March 9.—Dr. Popescu picked us up at 9:30 a.m. and drove us to the Institute for Social Studies for an appointment for my wife with someone at this Institute. This person could not be located so Dr. Popescu drove us to the Medical School for a meeting with Dr. Roman Vlaicu, Head, 1st Department of Clinical Medicine, Dr. Mircea Cucuianu, Dr. Pavel Pitea and their staff. An agenda was agreed to as to the order I would visit the various departments at the Medical School. Dr. Cucuianu, a clinical pathologist who teaches a post-graduate course in clinical medicine, showed me his laboratory and explained his work to me. Dr. Cucuianu had spent a year as a visiting scientist in the laboratory of Dr. Mustard in Canada. He spoke excellent English and German and can also speak French, Italian, Spanish and Russian. Dr. Cucuianu took part in a Ciba Symposium on Medical Education in Europe in 1973. His thoughtful analysis was printed in the collection of papers that were given by the representatives of the respective countries (a reprint of Dr. Cucuianu's paper is appended to this report). Dr. Cucuianu has published papers in the language of the respective countries of Russia, France, Spain and Germany, although most of his studies have been published in English in the leading journals in his area, such as the *Journal of Atherosclerosis*, *Biochemistry and Biophys. Acta* and the *Journal of Clinical Medicine*. He is a recognized, international authority on the influence of blood platelets in thrombosis and in the enzyme systems involved in lipoprotein synthesis.

March 10.—Dr. Popescu had arranged for my wife to see a representative of the History Department and then drove me to the Institute of Nutrition at which Dr. Pitea is director. This institute, in cooperation with the clinicians, had carried out a survey in seven different mountain villages (Table 1). Some of the villages were so remote that the survey team had to walk part way to the villages. The peasants were found to have low serum cholesterol levels and coronary heart disease was rare in spite of the fact that they ate butter and lard as culinary fats and ate more than one egg/day/capita. A listing of differences in food availability in Romania and the U.S.A. is given in Table 2.

March 11.—Dr. Popescu had again arranged for my wife to gather useful information on the educational system in Romania. As all of our three children are involved in education at either the high school or university level and we often compare notes on our experiences, her observations are of particular interest. Furthermore, as an elected member of the Champaign County Board and on the Youth Committee, she has further insight into comparative educational systems. She has taught high school English and Spanish at Kansas State University and Sociology at Parkland College in Champaign. Her report is included with mine.

Dr. Popescu took me to the office of Dr. Cucuianu as the latter had collaborated with my next contact, Dr. O. Berzu, Head of the Department of Biochemistry. Dr. Berzu has worked in the laboratory of Dr. A. Lehninger at Johns Hopkins University, Dr. Britton Chance at the Johnston Foundation at the University of Pennsylvania, and has corresponded with Dr. Henry Lardy, The University of Wisconsin at Madison. He has published extensively on basic work in cellular

biochemistry, oxidation, reduction processes in cell organelles, measurement of oxygen uptake and affinity of respiratory enzymes for oxygen and the relationship between structure and function of cell mitochondria.

A brilliant young man in his laboratory, Dr. G. Benga, had spent a year in the laboratory of Dr. D. Chapman, Department of Biochemistry, University of Sheffield in England, one of the top authorities on cell membrane composition and function. Dr. Benga published a paper on this subject entitled "Interpretation of the Electron Spin Resonance Spectra of Nitroxide-Maleimide-Labelled Proteins and the Use of this Technique in the Study of Albumin and Biomembranes" in BBA 400, 69, 1975. He would be able to work on an NSF project in the area of cell membranes. He and Dr. Cucuianu plan to collaborate on a study of red cell membranes from various population groups in Cluj.

March 12.—Dr. Cucuianu introduced me to Dr. B. Cuparencu, Director of Pharmacology; both have collaborated on joint studies. This laboratory was located directly across the square from the Napoca Hotel, which could have been a first class hotel in any country. Dr. Cuparencu is interested in drugs which control arrhythmia. This is the number one problem in a "heart attack" and an ideal drug for the control of arrhythmia is not available anywhere. The leading drug for this purpose in the U.S.A. is Propranolol; however, this drug sometimes has undesirable side effects. The high death rate in the first few hours after a "heart attack" represents the best proof of its limitation. A better drug to control arrhythmia would receive immediate use by every physician in the world.

March 13.—As this was Sunday, Dr. Cucuianu volunteered to drive us up a canyon near Cluj, which had been dammed to hold a water supply for Cluj and also served to generate electric power. We stopped at some picturesque villages on the way and spent the rest of the day writing letters.

March 14.—Dr. Cucuianu picked me up at 9:30 a.m. and I presented a 40 minute lecture, with the aid of slides, in the main auditorium at the First Department of Medicine. The audience was composed of students and staff. I talked briefly with each slide and Dr. Cucuianu translated my remarks into Romanian. There was a lively discussion of 30 minutes after the lecture. I spent the afternoon writing and reading the many reprints of publications that I had accumulated.

March 15.—Dr. Cucuianu picked me up again at 9:30 for another visit with the Nutrition group. As in Bulgaria and Hungary, the Romanian sunflower seed oil processors are wasting the tocopherol that is removed during the deodorization process. This distillate could be sold to Western Europe for broiler rations.

March 16.—Dr. Popescu and his wife drove us to Tirgus Mures for a visit with the staff of another medical school approximately 60 miles from Cluj. We were met at the Grand Hotel by Dr. Andre Horvath, Clinical Cardiologist and Dr. M. F. Kerekes, a biochemist at the medical school. Dr. Horvath told us that he had been practicing medicine in Tirgus Mures for over 30 years and that he had seen the rate of heart disease and diabetes steadily increase. A walk around the square near the hotel was instructive. One can walk past one sweet shop or liquor store after another. The only fruit we saw for sale were some small dried-up apples.

March 17.—Professor Horvath drove us to the main building of the medical school for a conference with 14 staff members in a beautifully furnished seminar room. Starting with Professor E. Mody, I was told of the research studies carried out by this group. Professor E. Mody believed that the level of glycoprotein influenced atherosclerosis. He determined total lipids and typed lipids by gel electrophoresis and also determined urinary glycoprotein on 200 patients, 75 men and 125 women 50–81 years of age. He found a strong interrelationship between glycoproteins and lipids. All of the patients suffered from coronary heart disease. Dr. Mody believed that glycoproteins show more essential modification than lipids. He found an increase in urinary glycoprotein without change in lipid in these patients. Fredrickson typing showed normal were 45 percent; Type I, 0.5 percent; Type IIa, 22 percent; Type IIb, 27 percent; Type III, 0.5 percent; Type IV or V, none. He centrifuged at 30,000 for 10 minutes and decanted the clear supernatant. The precipitation was soluble in alcohol. He also used “healthy” individuals and found in atherosclerosis more than double the amount of glycoprotein, that is, 6.0 percent normal binding of hexosamine loose bound to protein which increased to 12 percent in atherosclerosis. Disease was confirmed in 45 percent. He believes that modification of glycoproteins is important. On the other hand, similar observations 10 years ago in Cluj found them irrelevant to atherosclerosis.

Dr. E. Olosz, who worked in the metabolic clinic of the 2nd Medical School faculty at Targus Mures, measured the effect of diet on the level of magnesium (Mg) in blood. If the Mg is normal, he noted an improvement in the intima layer of the aorta. They ask themselves whether the diet of man is deficient in Mg and if increasing dietary levels of Mg can improve or repair the damage. They first assayed and observed in humans that one can't show a decrease or even a small increase in serum Mg and that the concentrations were still normal with no pathology. A second experiment was based on the observation of the Schroeder correlation between drinking water (H_2O) and Mg. Dr. Olosz found no correlation between the mineral content of water and hypertension and, therefore, there was no confirmation of Schroeder and Morrison. Dr. Olosz considers atherosclerosis mainly a disease of the vascular wall and difficult to study in vivo. He found a great difference in the vessel wall of patients; some patients show atherosclerosis only in the upper part of the body.

Dr. Bucha classified lipoproteins by the Fredrickson system after a fat tolerance test and found that the type could change with the test. In normal cases, there was no change. In hyperlipoproteinemia, one can change the type. Type IIa can change to Type IIb or IV and occurred more often in urban areas.

Dr. Brassai discussed the medical-clinical aspects of atherosclerosis of the lower limbs. In operative atherosclerosis, on the basis of clinical observations, they found 70 percent hyperlipoproteinemia and 30 percent normal serum lipid levels. The most frequent type was Type IIa and IIb. These results will be presented in Tokyo at the Cardiology Conference. Dr. Brassai believes that there are a lot of “normal” types which are not normal at all.

Dr. Monoki discussed the consultation service for the prevention of atherosclerosis. He has been studying the risk factors in atherosclerosis.

During the last five years, 5,000 people have been screened. After clinical and lipid screening, they selected 400 patients. Among these 400 patients, they found that 80 percent were Type IIa, there were only 2.5 percent with Type III and five patients were Type V. The patients were divided into three groups—one, without atherosclerosis, but with problems of risk factors, increasing body weight and smoking; two, those people with myocardial disease; and three, those with diabetes. Chloresterylamine lowered the lipid level in only a few patients. Clofibrate was best when used with Type IV. Dr. Monoki started this study five years ago.

Dr. M. F. Kerekes has surveyed plants and found garlic leaves to contain an agent which lowers lipid levels. There was a diminished cholesterol level of 10 percent. He also made an ethanol extract of garlic. Dr. Kerekes published this work in a recent issue of *Artery*. I believe it is possible that the garlic decreased food consumption and thus reduced serum cholesterol levels.

March 18.—Dr. Kerekes called for me at 9:30 a.m. and drove me to the medical school for a lecture in the main auditorium. As Dr. Cucuianu had effectively translated in Cluj, Dr. Kerekes translated my remarks at Tirgus Mures. However, the lively discussion with students and staff after my lecture took even more time than at Cluj.

March 19.—Dr. Horvath called for us at 9:00 a.m. and with Dr. Kerekes as an interpreter drove us to an old Saxon village, Sighisoara, and a resort area. Dr. Horvath stopped several times at hospitals in the villages we passed through to check with doctors at these hospitals. As at Cluj, the medical staff in the villages and cities in the Tirgus Mures area depended on the medical school for guidance.

March 20.—Dr. Monoki Stefan called for us at 9:00 a.m. and drove us back to Cluj in his car. Dr. Stefan with Dr. C. Bedo have studied the lumberjacks in the Transylvania mountains since 1950. In 1950, the diet of the lumberjacks in the winter was composed of 12 percent protein, 28 percent fat and 57 percent carbohydrates. In 1960, protein intake increased from 12 to 14 percent and fat intake decreased 3 percent. Today, protein intake has increased to 14.5 percent and fat intake to 30 percent. One quarter of the protein was supplied by animal products. In the summer, the lumberjacks ate a diet composed of 37 percent fat, 51 percent carbohydrates and 12 percent protein. Hypertension was noted in 6/1,000, coronary heart disease in 3/1,000 and gastric cancer in 1.8/1,000. However, death from coronary heart disease was less than 1/1,000, which is not the case of lumberjacks in Finland. WHO data indicates that the lumberjacks in Finland have the highest rate of acute myocardial infarction in the world. The lumberjacks in Romania and Finland both consume butterfat, lard, eggs and meat. However, those in Finland obtained 60 percent of their visible fat intake from hydrogenated fish oil; this product is not available to the lumberjacks in Romania.

The highway from Tirgus Mures to Cluj runs through the fertile Mures river valley. This valley could be growing more fruit trees on the steep slopes and not ploughed as is presently the case. A larger food industry could be developed in this area and strawberries, raspberries, cherries, peaches and apricots grown and canned or frozen. Most urban homes in Romania now have a refrigerator; the freezer compartment should contain frozen fruit so it can be eaten for dessert

instead of the sweets that are presently available. This industry could also generate many millions of dollars in hard currency. Western Europeans can use frozen fruits in the winter months too and improve their health. I noted trucks equipped with refrigeration units on the roads which indicates that this industry does exist in Romania. The canning industry could also be improved. I bought a jar of peaches and a jar of pears in a grocery store in Tirgus Mures. Both fruits had been picked green and cooked in glass jars. Better food technology would provide for better quality. One of my former students, Dr. O. Johnson, presently a Vice President at Hershey Corporation, told me at the Federation Meetings that his company had recently sold a 50 million dollar chocolate making plant to Yugoslavia. It would be wiser to buy canning and packing plants as the people in Europe need more fruit and vegetables in their diet and less chocolate. It is ironic that the controlled economy of an Eastern European country does not do any better for the nutrition of its people than Western Europe.

March 21-23.—On our return to Cluj, I told Dr. Popescu that I wanted to fly to Bucharest the next day in order to complete our visits and return home. However, he could not arrange a flight for us and suggested instead that he could drive us through the Oriental Carpathian Mountains and take a plane back to Bucharest from Suceava. I'm glad now that we were able to make this trip as the highway ran through very beautiful valleys and old villages. This trip provided for a different view of Romania than Cluj and Tirgus Mures. We stopped at a mountain village to admire the incredible skill and patience that was necessary to produce the embroidery that the women in this village showed to us. Surely, Romania is blessed with a talented people in even the remote areas of this country.

March 24.—Dr. Birligiu called for me at 9:00 a.m. with an Academy car and took me to Fundeni Hospital to visit with Dr. Pausescu. The hospital grounds housed two separate 600 bed hospitals and a research laboratory connected to a third hospital. Two of these hospitals were so damaged by the earthquake that they were evacuated. The laboratory was also damaged, but was still usable. This laboratory was equipped with a tiled operating room, which was as well stocked with instruments as any I have seen. It contained a heart-lung machine, an adjustable operating table and was mainly used for studies on dogs and pigs. Dr. Pausescu has worked out a method to keep isolated dog hearts beating for two months and was able to increase output of blood by various manipulations. He had focused on techniques to keep hearts viable for transplant operations. I suggested that he apply his technique to coronary patients and he agreed to cooperate with the clinical cardiologists at Fundeni Hospital. Next I visited Dr. Aurel Moga, President of the Medical Academy. Dr. Paun, as well as an interpreter, talked with me for almost two hours. I told Dr. Moga of my desire to prepare an NSF application for cooperative funding and suggested that Dr. Cucuianu would be helpful in the preparation of an NSF application. He volunteered to call Dr. Cucuianu and to tell him to come to Bucharest in order to help prepare an application for NSF funds. Unfortunately, Dr. Cucuianu did not come to Bucharest, as I had hoped for.

March 25.—I visited Dr. Mincu and two competent assistants, Dr. Constantin Dumitrescu and Dr. Stefan Andrian Georgescu, explained

their interest in peripheral circulatory diseases. I was told that the Pepsi Cola contained $\frac{2}{3}$ cyclamates and $\frac{1}{3}$ sugar as a sweetening agent. That afternoon I visited Dr. C. Velican and Dr. Steinbach in an extensively damaged hospital. Dr. Velican told me that in his opinion there had been no substantial contribution to the understanding of atherosclerosis for the last 15 years. In fact, he stated that he was completely puzzled by the disease process which he found different from cholesterol-induced atherosclerosis in animal models. Dr. Velican has written a book in English on atherosclerosis which was published by Verlag in Berlin.

Dr. Steinbach's home and laboratory were extensively damaged by the earthquake. However, he had managed to accept this loss. Dr. Steinbach has carried on extensive nutrition surveys of fishermen in the Danube Delta. He found that these fishermen consumed large quantities of fish in the summer and pork and lard in the winter. They used rowboats or sailboats rather than power boats; their rate of coronary heart disease was as low as the villagers in the remote mountain areas of Transylvania.

March 26.—I visited the laboratory of Dr. Mincu again and had a good discussion with Dr. Stefan Georgescu who had worked in Guy Hospital in London. I was told Pepsi Cola may not contain cyclamates. I spent the rest of the afternoon visiting Sid Smith, NSF attache at the US Embassy. We discussed how we could set up ways of getting Current Contents to Romanian researchers.

March 27.—Sid Smith invited us for dinner at his apartment and we spent the afternoon visiting the village museum in Bucharest and talking about the research proposal that I had decided to prepare.

March 28.—I visited the laboratory of Dr. Pausescu at Fundeni Hospital. He introduced me to Dr. Ion Ohra, a clinical cardiologist at the hospital. Dr. Ohra is a former President of the World Health Organization and was responsible for the data provided to WHO from Bucharest. He gave me a copy of the complete report entitled "Myocardial Infarction Community Registers, 1976. WHO, Copenhagen." Dr. Ohra told me that in 1920 the ratio of cerebral to coronary disease was 8/1; in 1975, the ratio had changed to 1/2 in Bucharest. From 1929–1944, he had personally been involved with 43 deaths and from 1948–1966 in 2,010 deaths from heart disease in Bucharest. In 1936, sugar consumption was 1 kilo/capita/year; now, it is 42 kilo/capita/year in Bucharest. Bread was substituted for millet in 1938 and meat consumption has increased from 7 kilo/capita/year in 1938 to 46 kilo/capita/year. Egg consumption is 245 eggs/capita in Bucharest and higher in the rural areas. Dr. Ohra is willing to cooperate on clinical studies and has the facilities to do so.

March 29.—I visited Dr. A. Petrovici at the Contacuzino Institute. He had collaborated with both Dr. Mincu and Dr. Velican and was responsible for the excellent electron microscopy photographs in their publications. He used a Hitachi-11 instrument which had been purchased in 1962. His technicians serviced this instrument, which is quite an achievement. I also visited briefly two Geriatric Institutes. One, the Institute de Gerontologie, 9 Rue Minastirea Caldarusani, was used by people over 60 years of age and the other near the International Airport was used as a health spa for foreigners with hard currency. We left

Bucharest on the 4:30 p.m. plane on a nonstop flight to London. We stayed in London overnight and flew to Washington on March 30.

March 31.—I stopped at the office of the National Academy of Sciences, the National Science Foundation and the office of Dr. Leavitt at the International Fogarty Center in Washington on my way back to Urbana. They were all interested in my observations in Romania. Dr. Leavitt was interested in developing contacts in Romania and xeroxed some of my calling cards that I had accumulated during my visit. I noted from the literature rack in the lobby that Dr. Ted Cooper was pictured with Russian cardiologists and that cooperative research projects are underway. Dr. Leavitt told me that an NIH site visitor team had stopped at Cluj in 1975, but cooperative projects had not developed from this visit. I had asked several of the researchers at Cluj, Tirgus Mures and Bucharest whether they had talked to anyone from the USA about their research. A group of physicians from the American Medical Association had stopped in Cluj in 1970, but they had visited the tourist attractions rather than the laboratories. It was evident that the researchers I had talked to at Cluj knew nothing of the NIH site visit, although the NIH site visit team had been interested in cancer rather than heart disease and, therefore, probably had not visited this section of the medical school.

TABLE I.—RESULTS OF SURVEY IN 7 VILLAGES IN TRANSYLVANIA, ROMANIA, IN 1962

Village	Number persons	Calories/day	Percent lipid in diet	Serum cholesterol (mg percent)	Total serum lipid
Marisel.....	412	2,895	20.0	137	721
Avram Iamu.....	94	2,990	23.0	140	804
Finigal.....	130	3,023	25.0	157	850
Corna.....	87	3,623	28.0	187	761
Sintana.....	171	3,883	34.0	176	709
Viaka.....	130	4,137	38.0	188	
Culenesti Oas.....	102	3,051	20.7	135	

Note: Margarine introduced in 1968; present consumption in urban areas equals 2 to 3 kilo per year per capita. These villages are presently being resurveyed. The results to date indicate an increase of 40 mg percent in serum cholesterol values.

TABLE II.—FOOD CONSUMPTION IN THE UNITED STATES AS COMPARED WITH URBAN AND RURAL ROMANIA

Item	United States per capita per year	Romania	
		Urban	Rural
Bread (pounds).....	1 75	201	281
Sugar (total) (pounds).....	1 102	56	32
Sugar (as soft drinks) (pounds).....	1 23	8	0
Hydrogenated vegetable fat (shortening) (pounds).....	2 14	0	0
Unhydrogenated vegetable oil (pounds).....	14	12	20
Margarine (pounds).....	10	3	2
Butter (pounds).....	6	24	12
Lard (pounds).....	5	2	8
Milk (quarts).....	229	121	101
Meat (beef, poultry, fish) (pounds).....	219	121	97
Eggs (number per year).....	279	760	1,141
Rate of myocardial infarction.....	6/1,000	1.5/1,000	0.3/1,00

¹ The bread in the United States is prepared from a highly refined flour and also contains emulsifiers which increase fat absorption from the intestinal tract. The bread in Romania is made from a nonrefined flour and contains no emulsifiers. An amino acid analysis of both flours shows no difference in composition. Egg consumption is more than 2 per day in some rural areas. Consumption data for United States from Dietary Goals for the U.S. Select Committee on Nutrition and Human Needs, U.S. Senate, February 1977. Consumption data for Romania from Dr. Orha and Dr. Pavel. The bread in Romania contains 5 percent added yeast.

² Estimate, accurate figures will be obtained. A comparison of population groups in Romanian villages with food consumption should provide more data than a diet survey in the United States as so much of the food in the United States is mass produced and of the same composition.

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN,
August 8, 1977.

Senator GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: I would like to call your attention to the quote in the enclosed clipping from the Champaign-Urbana Courier, July 27, 1977. "As public policy makers, our standard of proof must be different from that of the research scientist. When there is an overwhelming probability or consensus on a subject we have an obligation to make recommendations to the public." How can your standard of proof be different from that of a research scientist? A fact is a fact and the fact is that eggs do not increase the serum cholesterol levels as three recent independent studies have indicated. Please also check Dr. Herbert's FTC testimony this spring. He is a researcher at NIH in Bethesda. Our study was not supported by anybody. I simply obtained the cooperation of cardiologists and persuaded them to feed their patients eggs or a custard substitute. It did take over five years to get my article into print. There is no "overwhelming probability consensus." I served on the subcommittee on dietary fats of the AHA in 1968 and I can tell you that there was no "consensus", in regard to the role of dietary cholesterol in heart disease in the current amount consumed in the American diet and there still isn't today. As I have written to you before, please spend more funds on research and less on trying to bring life to "a dead horse."

Sincerely yours,

F. A. KUMMEROW,
Director, The Burnsides Research Laboratory.

Enclosure.

CHOLESTEROL CUTS CAUSE CONCERN FOR EGG INDUSTRY

WASHINGTON (AP).—The egg industry, saying it has been hurt by a Senate committee's recommendation that Americans cut down on cholesterol consumption, urged the panel Tuesday to withdraw the recommendation.

Nutrition Committee Chairman George McGovern, D-S.D., gave no indication that the recommendation would be withdrawn. Citing links between cholesterol and heart disease, he said, "It seems only prudent for Americans to reduce their dietary cholesterol."

Representatives of the United Egg Producers were protesting the panel's recommendation, made earlier this year, that Americans reduce cholesterol consumption, including by cutting down on eggs in the diet. The panel said one egg yolk by itself contains almost as much cholesterol as a person should eat in a day.

"We have felt the results of the cholesterol scare in our businesses," said Jack Dubose, a Gonzales, Tex., egg producer, appearing for the industry group. He said the recommendation "has the potential of putting many small, family farmers out of business."

Cholesterol is a waxy substance that accumulates in the arteries.

Studies have shown that persons with high levels of cholesterol are more likely to have heart attacks.

The egg producers said there is no clear proof that reducing egg consumption will reduce chances for heart disease.

"We don't believe this committee or any facet of the government should make a recommendation that would tend to destroy an important segment of the nation's agricultural economy without unimpeachable facts to back up its recommendation," Dubose said.

The testimony was supported by two doctors who also differed with the advice of many researchers to reduce cholesterol levels. Drs. Robert Olson of St. Louis University and Norton Spritz of the Veterans Administration Hospital in New York City said more evidence is needed for such a recommendation.

"In tests, cholesterol levels have been reduced. But that did not significantly lower mortality rates," Olson said. "Rather than spend federal money to promulgate what may well be erroneous information, we should carry out more research to be sure of what we are doing."

Their testimony was disputed by five Senators at the hearing, including McGovern. "As public policy makers, our standard of proof must be different from that of the research scientist. When there is an overwhelming probability or consensus on a subject we have an obligation to make recommendations to the public," McGovern said.

UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN,
June 14, 1977.

DR. PAVEL PITEA,
*Scientific Assistant Director, Institute of Public Health and Medical
Researches, Romania*

DEAR DR. PITEA: Please find enclosed a corrected table. Dr. Cucuianu indicated in a letter to me that your data had been calculated in grams/day. In order to have these data comparable to the American data, I recalculated them on the basis of pounds/capita/year. Romanians seem to eat more eggs and less meat. However, as you add 5% yeast to your bread, the protein intake may be comparable to that of Americans and the fat intake less. If you do not get the packing material for your GLC let me know. I'm sure your cooperation with Drs. Cucuianu and Popescu will provide some meaningful data.

Sincerely yours,

F. A. KUMMEROW,
Director, The Burnsides Research Laboratory.

Enclosure.

Dr. F. A. KUMMEROW,
Burnsides Research Laboratory, University of Illinois, Urbana, Ill.

DEAR DR. KUMMEROW: I have received your latest letter, dated June 14, 1977, with the corrected table. For reasons irrespective of my will I couldn't answer your letter dated June 6, 1977. I do it now mentioning that I have no more corrections to do on your latest table.

Thank you so much for the chromatographic data concerning the amino-acid content of the American flour as compared to the Romanian one.

No more than 3 eggs per day are consumed on the average by villagers in rural areas. The rate of myocardial infarction you provided is also correct.

Thank you for having sent us the gas chromatograph columns, but for the time being we haven't received them yet. We will let you know as soon as we receive your packing.

We hope for a future cooperation.

Sincerely yours,

Dr. PITEA PAVEL.



The influence of egg consumption on the serum cholesterol level in human subjects

F. A. Kummerow,¹ Ph.D., Youngja Kim,² M.D., Hull,³ M.D., J. Pollard,⁴ M.D., P. Ilinov,⁵ Ph.D., D. L. Dorossiev,⁵ M.D., and Jiri Valek,⁶ M.D.

ABSTRACT The influence of whole fresh eggs on the serum cholesterol level in men and women was studied independently in hospitalized patients in Sofia, Prague and Urbana-Champaign. The patients were fed two eggs or the equivalent of two eggs in a custard base or milk shake in addition to the foods that were consumed in their diet pattern. The serum cholesterol level was determined before and at periods varying from 5 hr to 54 days after the consumption of the eggs. The mixed fatty acid composition of the total lipids in the serum and the erythrocytes was also determined. In the majority of patients, the serum cholesterol level did not change significantly 5 hr after the consumption of 465 mg of cholesterol in an egg custard base or milk shake or after up to 54 days of continued consumption of two whole eggs per day. The serum cholesterol level of some subjects increased and others decreased at all three experimental sites. A comparison of the mixed fatty acid composition of the total serum lipids obtained from men and women who had received treatment for other reasons than cardiovascular disease with those that had been treated for cardiovascular disease indicated that the serum from both groups contained a substantial amount of polyunsaturated fatty acids. The lipids extracted from the red blood cells obtained from patients in Urbana-Champaign and Sofia did not differ significantly in linoleic and arachidonic acid content. *Am. J. Clin. Nutr.* 30: 664-673, 1977.

A low saturated fat/low cholesterol diet has been recommended as one of the most effective means of controlling serum cholesterol levels (1). As an egg contains a relatively large amount of cholesterol (approximately 250 mg/100 g), less consumption of eggs has been suggested (2-4) as a means of lowering serum cholesterol levels. However, a decreased per capita consumption of 123 eggs since 1945 (5) has not decreased the total daily cholesterol intake in the United States as the per capita consumption of meat and dairy products has increased. Calculations based on per capita food consumption data since 1909, the date such information first became available (6), and the cholesterol content of the individual food item (7), indicate that the total daily cholesterol intake as furnished by meat, dairy products, and eggs equaled 545 mg in 1909, 614 mg in 1960, 602 mg in 1965, and 600 mg in 1973 (Table 1). Furthermore,

because of an increased consumption of chicken fat, which contains six times more linoleic acid than beef fat (8), the composite mixture of "invisible" fat in animal food products actually supplied 0.7 pounds more linoleic acid/capita per year to the diet in 1975 than it did in 1909.

The composite mixture of "visible" fats in the American diet has also changed in composition. In 1909, lard, beef tallow, and butterfat furnished the main source of culinary fat; a portion of the beef tallow was mixed or compounded with cottonseed oil

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TABLE 1
Annual per capita consumption of animal food products

Year	Meat		Poultry		Fish		Eggs		Dairy products		Animal fat		Total pounds of linoleic acid	Total cholesterol ^b
	Pounds	Pounds of linoleic acid ^c	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid		
1909	146.6	0.70	15.9	0.38	13.9	0.47	35.1	0.63	178	0.18	12.4	0.43	2.8	545
1960	146.9	0.71	34.6	0.83	13.2	0.45	42.5	0.76	238	0.24	7.5	0.26	3.3	614
1961	145.9	0.70	37.8	0.90	13.7	0.47	41.7	0.75	235	0.24	7.4	0.26	3.3	563
1962	147.1	0.71	37.4	0.90	13.6	0.46	41.4	0.75	235	0.24	7.3	0.26	3.3	609
1963	152.0	0.73	37.9	0.91	13.7	0.47	40.4	0.73	234	0.23	6.9	0.24	3.3	610
1964	155.7	0.75	38.9	0.93	13.5	0.46	40.4	0.73	235	0.24	6.9	0.24	3.4	616
1965	148.3	0.71	41.3	0.99	13.8	0.47	39.8	0.72	234	0.23	6.4	0.22	3.3	602
1966	151.4	0.73	44.3	1.1	13.9	0.47	39.7	0.71	234	0.23	5.7	0.20	3.4	607
1967	158.3	0.76	46.2	1.1	13.6	0.46	40.6	0.73	230	0.23	5.5	0.20	3.5	623
1968	162.4	0.78	45.8	1.1	14.0	0.48	40.1	0.73	231	0.23	5.7	0.20	3.5	628
1969	161.4	0.77	47.8	1.1	14.2	0.48	39.3	0.71	230	0.23	5.4	0.19	3.5	633
1970	164.6	0.79	50.1	1.2	14.8	0.50	39.5	0.71	226	0.23	5.3	0.19	3.6	628
1971	170.0	0.82	50.3	1.2	14.4	0.49	39.9	0.72	228	0.23	5.1	0.18	3.6	639
1972	166.5	0.80	52.5	1.3	15.3	0.52	39.0	0.70	228	0.23	4.9	0.17	3.7	631
1973	154.6	0.74	50.5	1.2	15.6	0.53	37.2	0.67	229	0.23	4.8	0.17	3.5	600

^a Calculations of pounds of linoleic acid based upon assumption that amount of linoleic acid in certain foods has not changed over the past 60 years. (Fat Content and Composition of Animal Products, The National Research Council, December, 1974). ^b Milligrams per day as calculated from the total per capita intake of each food item and its cholesterol content (J. Am. Oil Chemists' Soc. 27: 414, 1950).

and sold as margarine. Shortenings made from hydrogenated vegetable oils did not become available until 1911 (9), and the ratio of the consumption of animal to vegetable fats has continued to change at an accelerated rate since that date. For example, the intake of visible animal fats has decreased from 21.9 in 1950 to 10.2 pounds/capita per year in 1975 and the intake of vegetable fat has increased from 24.0 to 43.1 pounds during the same time period (10). Approximately two thirds of these 43 pounds of vegetable fat was hydrogenated or converted to a "saturated" fat in order to stabilize it against oxidation.

As many epidemiological studies have provided valuable data (11-18), it seemed of interest to compare serum cholesterol levels of Americans with those of Czechs or Bulgarians who have not substantially increased their per capita hydrogenated fat intake but have increased their per capita egg intake. The consumption of eggs has increased from 248 to 301 in Czechoslovakia and from 127 to 163 in Bulgaria (R. E. Anderson, Jr., personal communication, Foreign Commodity Analysis, USDA, Washington, D.C.) and has decreased from 314 to 279 in the United States from 1971 to 1975 (5). In the present study, the effect of eggs on convalescent patients from three local hospitals in Urbana-Champaign was compared to the effect of eggs on similar patient groups in Prague and Sofia.

Material and methods

In Urbana, two groups of human subjects were used: a group of 30 randomly selected volunteer hospital patients suffering from cardiovascular disease and a group of 30 randomly selected volunteers in the hospital for reasons other than cardiovascular disease. The latter group did not include patients with diabetes, obesity, liver disease, intestinal problems, or lipid abnormalities. Blood samples, 5 ml, were taken before breakfast at 8:30 AM and again after breakfast at 11:30 AM. The dietary source of cholesterol was then consumed and a 5 ml blood sample was taken at 4:30 PM. Whole pasteurized eggs in a flavored milk shake or mixed with a custard base was used as a source of cholesterol. The custard was prepared from 1 cup (6 ounces) custard base (Delmark Quick Egg Custard Mix, Delmont Co., Minneapolis, Minn.) and $4\frac{3}{4}$ cups skim milk; $4\frac{2}{3}$ ounces of this mix, and $3\frac{1}{3}$ ounces of whole pasteurized eggs (Gerber Products Co., Fremont, Mich.) were blended together, chilled, and served to provide 465 mg of cholesterol in each serving.

The milk shake contained an equivalent amount of cholesterol. The hospital menu of 1,990 cal contained 78 g of protein, 94 g of fat, and 208 g of carbohydrate with a minimum of 340 cal from skim milk, 200 cal from bread or cereals, 135 cal from margarine, 150 cal from fruits or vegetables, and 4 ounces of lean meat/day in addition to the flavored milk shake or custard. Cholesterol determinations were carried out according to the method of Zak et al. (19). The mixed fatty acid composition of the total lipids in the serum and in the erythrocytes was determined as previously described (20, 21). The chloroform-methanol that was used to extract the lipid contained 0.01% α -tocopherol; all manipulations were carried out under nitrogen.

In Prague, a group of 21 patients who had been hospitalized for at least 1 week was used. No patients with malignancies, cardiac decompensation, unstable angina pectoris, or postoperative status were included. The diet was prepared in the metabolic kitchen from commonly used food components in Prague. It furnished daily 250 mg of cholesterol and $2,400 \pm 180$ cal of which 40% was supplied by fat. The fat contained 42.5% polyunsaturated fatty acid, 32.5% monounsaturated, and 25% saturated fatty acids. The cholesterol was furnished by the blending of two fresh eggs into a soup that was provided as part of the midday meal; less than one kilo of fluctuation in weight of the average patient was noted during the hospital stay. Blood samples were obtained after at least a 12-hr fast. The serum cholesterol and triglyceride levels were determined according to the method of Grafnetter et al. (22, 23) and lipoprotein phenotyping was determined by electrophoresis (24).

In Sofia, two groups each of twenty patients who had been operated on for inborn or acquired heart defects were fed a diet of 2,330 cal in four meals consisting of: 96 g of protein, 77 g of fat, and 295 g of carbohydrate. The protein was supplied as beef or chicken, the fat as sunflower oil, and the carbohydrate as bread, high starchy foods or desserts. No hydrogenated vegetable fat was used in these food items as such fats are not available in Bulgaria. Two whole eggs were added at lunch to the patients on this convalescent diet. Three milliliters of blood were drawn after a 12- to 14-hr fast and the serum cholesterol assayed according to the method of Watson (25). The total lipid level of the serum was determined photometrically (26). The percentage composition and cholesterol content of the three basal diets is listed in Table 2.

TABLE 2
The percentage composition, total calories, and cholesterol content of the three basal diets

	Urbana	Prague	Sofia
Protein	20%	20%	20%
Fat	40%	40%	17%
Carbohydrate	40%	40%	63%
Total cal	1,990	2,400	2,330
Cholesterol mg/day	600	250	600 ^a

^a Variable, from 400 to 600 mg/day.

TABLE 3

Dynamic changes in mg/100 ml serum cholesterol and mg/100 ml total lipids of patients in Sofia on the convalescent diet (A) and of patients^a eating 2 eggs in addition to this diet (B)

Clinic no.	Sex	Age	0 Days		7-35 Days		20-54 Days	
			Serum cholesterol	Total lipid	Serum cholesterol	Total lipid	Serum cholesterol	Total lipid
Patients on the convalescent diet (A)			20-39 Days					
794	F	37	270	1150			230	720
836	F	43	210	600	250	780 ^b	225	600
847	F	47	360	1150	280	930	330	1380
902	F	50	210	810			250	840
934	F	30	245	630	250	730	140	510
936	F	57	235	690	300	1000	215	840
975	F	29	250	880	200	960	295	
960	F	27	160	630			180	780
981	F	36	270	780	180	810	315	1000
848	M	24	220	630	205	660	220	660
872	M	32	260	840	200	870 ^c	230	930
904	M	22	160	660	185	690	195	750
993	M	50	220	690			210	730
251	M	51	350	1400			330	1300
295	M	19	200	780			170	700
307	M	21	180	570			160	540
416	M	21	175	480			225	810
417	M	33	275	960	220	1000	280	900
438	M	25	180	630	210	690	225	900
439	M	28	180	600	200	660	190	670
Average	20	34 ± 11	231 ± 56	778 ± 232	223 ± 38	815 ± 133	231 ± 55	819 ± 225
Patients on the convalescent diet + 2 eggs/day (B)								
788	F	27	180	650	200	630	210	570
789	F	39	320	840	310	1000	280	800
835	F	24	240	540	190	900 ^d	210	690
838	F	33	360	1000	320	960 ^e	360	1000
869	F	47	370	1800			360	1700
871	F	43	300	1000	305	780	320	1000
874	F	36	310	1100	330	1000	240	810
937	F	36	270	600	310	900	180	570
938	F	29	210	720	230	780	240	900
795	M	36	160	600	230	900 ^f	310	960
796	M	25	180	590	175	630	160	510
905	M	39	240	720	235	510	210	600
1024	M	32	225	690	250	840	270	840
1007	M	50	230	660	225	780 ^g	260	840
1471	M	51	270	1100			300	
1466	M	40	285	960			290	
308	M	42	240	780	250	630	280	960
373	M	33	290	990	250	930	300	1000
415	M	30	290	780	300	840	320	960
432	M	25	250	1000	250	800	220	650
Average	20	36 ± 8	261 ± 57	856 ± 287	256 ± 48	812 ± 143	266 ± 56	853 ± 269

^a Diagnosis, atrial septal defect; ductus arteriosus persists; mitral stenosis; ventricular septal defect; stenosis arteriae pulmonalis—post operative, 28 days or more. ^b At day 23, cholesterol = 245, total lipids = 900. ^c At day 17, cholesterol = 210, total lipids = 690. ^d At day 19, cholesterol = 230, total lipids = 750. ^e At day 21, cholesterol = 350, total lipids = 1200. ^f At day 22, cholesterol = 275, total lipids = 1000. ^g At day 45, cholesterol = 225, total lipids = 840.

Results

In the majority of patients, the serum cholesterol level did not change significantly either after 5 hr or after up to 54 days of continued consumption of two whole eggs

or 465 mg of cholesterol in an egg custard base or milk shake. In Sofia, the average serum cholesterol of 231 ± 56 mg/100 ml remained unchanged and the total serum lipid level increased from 778 ± 232 mg/100 ml to 819 ± 225 mg/100 ml in 20

TABLE 4
Dynamic changes in serum cholesterol and triglyceride levels of patients in Prague on the convalescent diet (A) and the same patients on this diet plus 2 eggs/day for another 7 days diet (B)

Clinic no.	Sex	Age	Convalescent diet (A)				Diet A + 2 eggs/ day (B)				Phenotype or diagnosis
			0 days		7 days		7 days		7 days		
			Serum cholesterol	Triglyceride	Serum cholesterol	Triglyceride	Serum cholesterol	Triglyceride	Serum cholesterol	Triglyceride	
86/73	M	53	282	217	278	100	242	143		HLP ^a IV	
578/72	M	26	210	258	244	182	227	157		HLP II	
53/73	M	51	258	93	272	114	235	132		HLP II	
559/72	M	44	205	71	212	64	199	132		HLP IV	
573/72	M	52	235	121	206	153	209	132		HLP IV	
546/72	M	46	266	93	227	132	206	114		HLP IV	
556/72	M	38	287	300	258	186	261	114		HLP IV	
608/72	M	44	353	600	278	271	262	230		HLP II	
628/72	M	42	372	942	293	443	353	859		HLP IV	
652/72	M	49	276	450	276	450	227	307		HLP IV	
622/72	M	36	206	228	151	114	179	115		Asthemia	
617/72	M	51	384	164	295	86	321	67		HLP II	
605/72	F	37	375	79	384	114	356	100		HLP II	
165/73	M	57	282	243	262	184	311	184		HLP II	
184/73	M	38	256	—	234	—	261	—		M. Buerger	
195/73	F	47	299	205	336	205	293	177		HLP II	
423/73	F	53	258	110	205	98	241	123		Neurosis	
435/73	M	53	227	125	177	129	184	181		HLP IV	
433/73	M	47	214	135	225	154	281	91		HLP II	
462/73	F	50	234	168	250	109	273	95		Neurosis	
445/73	M	43	246	285	216	169	192	252		Duod. ulcer	
Average	21	46 ± 7	273 ± 56	173 ± 104	251 ± 53	185 ± 169	253 ± 52	220 ± 203			

^a Hyperlipoproteinemia.

patients fed the convalescent diet for a period of time which varied from 20 to 39 days (Table 3). The serum cholesterol level increased from 261 ± 57 mg/100 ml to 266 ± 56 mg/100 ml and the total lipid level decreased from 856 ± 287 mg/100 ml to 853 ± 269 mg/100 ml in 20 patients fed two eggs/day in addition to the same convalescent diet for a period of time which varied from 20 to 54 days. The serum cholesterol and total serum lipid levels increased in some patients and decreased in others; the serum cholesterol level in one patient in each group changed by more than 100 mg/100 ml.

In Prague, the average serum cholesterol level decreased from 273 ± 56 mg/100 ml to 251 ± 53 mg/100 ml and the triglyceride levels increased from 173 ± 104 mg/100 ml to 185 ± 169 mg/100 ml in the 21 patients fed the convalescent diet for 7 days (Table 4). As in Sofia, when these patients were fed 2 eggs/day for 7 days, in addition to the convalescent diet, the serum cholesterol level increased in some patients and decreased in others. The serum cholesterol level increased an average of 2 mg/100 ml

or from 251 ± 53 mg/100 ml to 253 ± 52 mg/100 ml and the triglyceride level increased from 185 ± 169 mg/100 ml to 220 ± 203 mg/100 ml. No apparent relationship was noted between the response to eggs and the lipoprotein phenotype.

In Urbana, the serum cholesterol level of only four out of 60 subjects changed more than 20 mg/100 ml 5 hr after the consumption of eggs in addition to the regular diet (Table 5). The serum cholesterol level of 15 men hospitalized for reasons other than cardiovascular disease increased an average of 7 mg/100 ml and of 15 women decreased an average of 3 mg/100 ml or from 174 and 228 mg/100 ml before to 181 and 225 mg/100 ml, respectively, 5 hr after the consumption of an amount of cholesterol equivalent to two eggs. Similar results were obtained with the patients suffering from cardiovascular disease. In this somewhat older group of patients, the serum cholesterol level of 15 men increased an average of 7 mg/100 ml and of 15 women decreased an average of 11 mg/100 ml or 182 to 189 and 197 to 188 mg/100 ml, respectively, after the consumption of an amount of cholest-

TABLE 5

Comparison of cholesterol and mixed fatty acids in serum lipids before and 5 hr after a test meal in Urbana^a

	Noncardiovascular		Cardiovascular	
	Male	Female	Male	Female
Average age	46 \pm 4	61 \pm 3	59 \pm 5	71 \pm 3
Serum cholesterol (0 hr) mg/100 ml	174 \pm 10	228 \pm 13	182 \pm 11	197 \pm 13
Serum cholesterol (5 hr) mg/100 ml	181 \pm 8	225 \pm 14	189 \pm 9	188 \pm 13
Serum fatty acids (0 hr)				
C14:0	1 \pm 0.2%	0.6 \pm 0.1%	1 \pm 0.1%	0.7 \pm 0.1% ^b
C16:0	40 \pm 3.0	51 \pm 5.0	42 \pm 2.0	40 \pm 2.0
C16:1	2 \pm 0.3	2 \pm 0.6	2 \pm 0.3	2 \pm 0.3
C18:0	7 \pm 1.0	4 \pm 0.6	7 \pm 1.0	6 \pm 0.6
C18:1	24 \pm 2.0	19 \pm 1.0	25 \pm 2.0	24 \pm 1.0
C18:2	22 \pm 2.0	16 \pm 3.0	18 \pm 2.0	22 \pm 2.0
C20:3	0.5 \pm 0.3	0.5 \pm 0.2	0.03 \pm 0.03	0.2 \pm 0.1
C20:4	3 \pm 0.5	5 \pm 0.2	4 \pm 1.0	4 \pm 0.5
Fatty acids (5 hr)				
C14:0	1 \pm 0.2	0.6 \pm 0.1	1 \pm 0.2	1 \pm 0.1
C16:0	39 \pm 3.0	47 \pm 3.0	46 \pm 5.0	43 \pm 3.0
C16:1	2 \pm 0.7	2 \pm 0.4	3 \pm 1.0	3 \pm 0.6
C18:0	8 \pm 1.0	6 \pm 1.0	6 \pm 1.0	6 \pm 1.0
C18:1	24 \pm 2.0	21 \pm 1.0	24 \pm 1.0	23 \pm 1.0
C18:2	23 \pm 3.0	18 \pm 1.0	16 \pm 3.0	21 \pm 1.0
C20:3	0.2 \pm 0.2	0.0 \pm 0.0	1 \pm 1.0	0.1 \pm 0.1
C20:4	3 \pm 0.0	5 \pm 1.0	4 \pm 1.0	3 \pm 0.6
L/O ratio (0 hr)	1 \pm 0.2	0.7 \pm 0.1	1 \pm 0.1	1 \pm 0.1
L/O ratio (5 hr)	1 \pm 0.1	0.9 \pm 0.1	1 \pm 0.1	1 \pm 0.1

^a Noncardiovascular versus cardiovascular, not significant. ^b SEM.

terol equivalent to two eggs. As no significant differences in serum cholesterol levels were noted between samples taken at 8:30 and 11:30 AM, only the values at 11:30 AM were listed in Table 5.

A comparison of the mixed fatty acid composition of the total serum lipids obtained in Urbana-Champaign from the patients who had received treatment for other than cardiovascular disease with those that had been treated for cardiovascular disease indicated that the serum from both groups contained a substantial amount of polyunsaturated fatty acids. The serum obtained from convalescent noncardiovascular men contained $22 \pm 2\%$ linoleic, $0.5 \pm 0.3\%$ eicosatrienoic, and $3 \pm 0.5\%$ arachidonic acid (Table 5). The fatty acid profile in the noncardiovascular women or the men and women cardiovascular patients did not differ significantly from these values. The lipids extracted from the red blood cells from these four groups of patients also did not differ significantly. They contained more arachidonic and palmitic and less linoleic acid than the serum. The lipids extracted from the red blood cells contained $19.6 \pm 0.2\%$ linoleic, $4.2 \pm 0.5\%$ arachidonic, $0.5 \pm 0.5\%$ eicosatrienoic, $26.6 \pm 1.9\%$ oleic, $13.0 \pm 0.2\%$ stearic, and $35.4 \pm 2.9\%$ palmitic acid. In Sofia, the lipids extracted from the red blood cells from ten apparently normal patients contained $11.3 \pm 2.1\%$ linoleic and $7.9 \pm 2.7\%$ arachidonic acid and those from eleven hyperlipemic patients contained $6.2 \pm 1.6\%$ linoleic and $4.5 \pm 1.4\%$ arachidonic acid.

Discussion

The nutritionally complete diets that were used in Sofia, Prague, and Urbana-Champaign may be the explanation for the insignificant changes in serum cholesterol levels that were noted after the consumption of an amount of cholesterol equivalent to two eggs/day. All of the dietary components had been a regular part of the diet and did not introduce variables known to influence serum cholesterol levels such as a lack of fiber (27), a change in nutrient bulk (28), a change from a solid to a liquid diet (29), a change in dietary fatty acid composition (30), or an excessive level of dietary fat

(31). Furthermore, unlike previous studies (29, 31-34), whole eggs rather than egg yolk powder or crystalline cholesterol were used in the present study. Egg yolk powder contains more cholesterol than whole egg powder or 3960 and 2400 mg/100 g, respectively (7). Egg yolk powder is therefore a more concentrated source of dietary cholesterol than whole egg powder for experimental studies. However, whole eggs rather than egg yolk are normally used in meal preparation. The egg yolk in two medium sized fresh eggs furnishes only 5.4 g of protein as compared with 11.7 g of protein for the whole egg (Table 6). Even though two medium sized fresh whole eggs contain only 11.7 g of protein, they contain, except for methionine and phenylalanine, the approximate total daily requirement for all eight of the essential amino acids (35). Two fresh egg yolks do not provide enough protein to satisfy the total daily amino acid need for any of the eight essential amino acids, although two fresh egg yolks contain as much cholesterol as two fresh whole eggs (36). In spite of the presence of other sources of protein (29-34), someone eating two whole eggs/day would be less likely to be deficient in any of the essential amino acids than someone eating egg yolk.

Amino acids are essential for the building of the apolipoproteins which "carry" the

TABLE 6
Essential amino acids required by man per day and in whole eggs or egg yolks


Amino acid ^a	Required (g) ^b	2 Medium sized, shell-free, whole eggs (96 g) ^c	2 Medium sized egg yolks (34 g) ^c
Isoleucine	0.70	.81	.37
Leucine	1.10	.99	.45
Lysine	0.80	.80	.39
Methionine	1.10	.39	.13
Phenylalanine	1.10	.63	.25
Threonine	0.50	.64	.33
Tryptophane	0.25	.22	.10
Valine	0.80	.96	.40

^a Composition of amino acids in fresh whole eggs and fresh egg yolks, from: Everson, Gladys J. and Helen J. Souders. Composition and nutritive importance of eggs. J. Am. Dietet. Assoc., 33: 1244, 1957. ^b W. C. Rose, R. L. Wixom, H. B. Lockhardt and G. F. Lambert. J. Biol. Chem. 217: 987, 1955. ^c Whole eggs, 11.7 g of protein and egg yolks, 5.4 g of protein, based on percent of protein in fresh whole eggs and fresh egg yolks: Nutritional Data. Harold A. Wooster, Jr. and Fred C. Blank, Heinz Nutritional Research Division, Pittsburgh, 1950. p. 86.

cholesterol in the blood (37, 38). An arginine-rich apoprotein has been found in the serum of patients with type III hyperlipoproteinemia and in animals fed an excessive amount of cholesterol (39). This arginine-rich apoprotein has more nonpolar and polar groups capable of combining with more cholesterol and phospholipid than normal apolipoprotein (38) and therefore increases serum cholesterol levels. It has also been shown in previous studies (40-42) that a balanced dietary amino acid level resulted in a lower serum cholesterol level than an imbalanced amino acid level (43). For example, chicks kept for 7 days on a diet containing synthetic amino acids plus 1.38%, 1.74%, or 2.82% arginine had serum cholesterol levels of 120, 103, and 125 mg/100 ml, respectively. Similar differences in serum cholesterol levels were noted after the deletion or excess addition of serine, alanine, leucine, lysine, proline, or methionine. The serum cholesterol level may, therefore, be as dependent on the amount and quality of dietary protein as on the source and dietary cholesterol levels that have been used in previous experimental designs (29, 31-33). None of these experimental designs recognized that the results obtained with egg yolk powder do not necessarily reflect the results that might have been obtained with whole eggs and should, therefore, not be projected to diet recommendations for human subjects (1-5). A recent study with whole eggs corroborated this viewpoint (44).

Haganfeldt et al. (45) have reported that patients who had suffered a myocardial infarction had lower concentrations of free octadecatrienoic and arachidonic acids and a higher concentration of eicosatrienoic acid in the plasma as compared to the controls. However, these data may only indicate that the culinary fats that are used in Sweden are more deficient in linoleic acid than culinary fats that are used in the United States or Bulgaria. The subjects that were used in the present study were not deficient in linoleic acid. The linoleic acid level of the serum and erythrocyte lipids obtained from the blood of convalescent patients suffering from cardiovascular disease did not differ significantly from the patients who had received treatment for other than cardiovascular dis-

ease and was similar to the level reported in the National Diet Heart Study (3). Variation in the mixed fatty acid composition of the total serum lipids indicated that some patients had consumed more linoleic acid than others. Although it has been shown in numerous studies (46-48) that individual dietary fats have a quantitative effect on serum cholesterol levels, our data, and data provided by the National Diet Heart Study seems to indicate that the serum level of linoleic acid is no different in the United States than the level noted in Bulgaria (P. Ilinov, personal communication; see also Ref. 26). This observation does not preclude the possibility that the kind of polyunsaturated fatty acids in cell membranes is important to the function of such membranes (49, 50) and may be relevant to cardiovascular disease.

It would seem desirable to test the response of a particular patient before assuming that the serum cholesterol level will increase when whole eggs are included in the diet of that patient. Such a test would eliminate uncertainty and provide for a wider choice of food items than the present recommended protocol provides (1-4). However, it may be advantageous to run more than one cholesterol determination in order to obtain reliable information on a specific subject's response to a source of dietary cholesterol. The results obtained in Sofia and in Prague, as well as those noted in previous studies (29, 30, 33, 34) indicate that in some individuals a simple change in diet regime per se influences their serum cholesterol level. 

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DETAILED REPORT BY A. L. KUMMEROW

I asked to visit programs for preschool children, for teenagers, and for elderly retirees. Schools visited were two kindergartens (for children age 3-6), one infant center (for children age 0-3), and one high school (14-18 years of age) taught in the English language. These were all in Cluj-Napoca in the Transylvania area of Romania. In Bucharest, my husband and I talked with some staff members at a training institute for geriatrics. We also visited a health spa for elderly people, but this was completely for foreigners with hard currency and did not represent my interests.

I was accompanied to the two kindergartens by their district inspector and my host-translator. The first kindergarten had 145 children, the second 240. The children were divided into groups of 25 by age with two educators per group. Teacher trainees and educators for a special area of interest also assist.

At the first kindergarten, one group of children was putting together a house or apartment from pieces of paper cut in rectangles, squares, and triangles. A second group was shaping a fish from soft copper wire. A plastic fish and a fish shaped from clay were on the table as models. I was shown a picture that they had made with pieces of cloth and framed to give to their mothers for Mothers Day. The class learning English greeted me in English and sang "... clap your hands and turn about ...". Then it was free time and the children happily chose areas of interest about the room. Small cloth partitions about the childrens' height were decorated to indicate play areas, such as doctor's office, doll puppet theater, tea time, and friseur. Friseur was very popular; the children put rollers in each other's hair, sat under "dryers," etc. Trucks, building blocks, and a wide variety of equipment was available for play.

At the second kindergarten, the children were out in the large park-like playground when we arrived. I was shown through the rooms, including the dining room, toilet area, shower and wash rooms, as well as class activity rooms. Built in sleeping pads for rest time folded into the walls. The equipment and supplies included many natural materials, which are emphasized (all kinds of seeds, pieces of wood, sheep wool, and plants). The supply cabinets and the illustrations and learning helps about the rooms made me think of Sesame Street on U.S. T.V. The parents also help purchase equipment and made equipment for the playgrounds. Both kindergartens had T.V. for use in visual aids.

My impression of these two kindergartens was that I must really be getting the deluxe tour and that the parents of these children must really be motivated for good education for their children. But subsequent inquiry and other schools that I saw, but did not visit in depth, led me to believe that while these two were probably outstanding, they were still typical of programs provided for children. Many, perhaps, would not have that much play area, particularly in Bucharest, but the programs on all levels are standardized through the Ministry of Education.

At each kindergarten I talked with the inspector and the director for at least an hour about kindergarten programs. The parents may

request special classes for their children in foreign languages, gymnastics, etc., or they may send their child to a kindergarten where all activities are conducted in a particular foreign language. A small fee of several dollars a month is charged for special classes, if the parents can pay, or nothing at all if the parents have four or more children. If the special school is not available where the parents live, then the child may stay in a boarding school connected with the desired school. Small villages, for example, do not have special language schools or other specialization.

A manual prepared by the Ministry of Education, of which I was given a copy, details the programs and activities for kindergarteners. The amount and kind of program activities vary with the age of the child and including the following:

1. Activities relating to nature and natural surroundings.
2. Speech development.
3. Mathematical activities.
4. Moral, political, and patriotic education.
5. Practical activities (develop coordination, use of hands, etc.).
6. Art—pictures and drawing.
7. Musical activities.
8. Physical education.

Three meals a day were served. The parents may bring their children between 5:30 and 6:30 a.m. or whenever the parents go to work. The children must be there between 8:00 and 8:30. There are also kindergartens for only three or four hours per day, if that is what the parents wish. All of the children wear light blue pinafores or jackets, which are left at school.

We briefly looked at an infant center located in one part of the building at the number two kindergarten. The infants were all in their cribs for rest time; many of them were still awake, but none were crying. They seemed to be contented children and the attendants seemed really to like them. A nurse checks the children daily and a medical doctor gives a checkup and records their weight once a month. If a child is ill, the mother is excused from work to stay home with the child.

HIGH SCHOOL—GRADES 8-12

I talked with the inspector, the director, and four teachers at a high school with instruction in English. I toured the classrooms, saw the industrial work, and visited an English grammar class. Compared to the U.S., discipline is an insignificant problem in Romanian schools. At 14, 16, and 18 years, students may take examinations and choose an industrial school or continue with a classical education. If there are enough places, one may have a choice, otherwise examinations must be taken. One must pass an examination to enter the university.

All of the students work one week per month in industry. Prior to January, 1977, they worked one day a week. This week may be spent in the school shop producing something needed in industry. The school I visited was making armatures in the school shop. The school is paid for this work and the money is used for special projects for the school. School is six days a week from 7:50 a.m. to 1:00 p.m.

Patriotic work is required of all the students. This may include helping with harvest or cleaning parks. We saw groups of school children with hoes over their shoulder going from villages out to the country on Sunday apparently to help with planting vegetables. In Bucharest, students were helping with the cleanup after the earthquake.

Children having difficulty in school are given help by the teacher and/or by other students, and, if appropriate, they may be encouraged to take different work. Socialization teaches respect for teachers and adults. The young Englishman who had taught the English conversation class of 11½ years told me he had never heard a teacher raise a voice against a student. There is almost universal respect and liking for teachers. Corporal punishment is not allowed.

All children have regulation clothes that must be worn to school. Also, clothes must have the student identification by district and school number and the student's number. Adults seeing students misbehave may report the student to his school where a discipline committee deals with it. The student may get his head shaved. I saw none.

Grading is on a scale of 1-10. Recognition is given to good grades and special work projects are exhibited. Teachers work with students on a volunteer basis during afternoons in special interest groups when desired by the students.

My impression was that though teachers in Romania work a long day, they are not subject to the emotional exhaustion that comes from attempting to maintain discipline. I also doubt that Romanian schools have the amount of paperwork that U.S. schools have. Most decisions are made by the Ministry of Education, I assume, and teachers are leaders in carrying out the program determined by the ministry. The socialization process does not at the present time place the youth peer group in opposition to adults. Parents, youth, and teachers seems basically in agreement on values. Student help to each other is strongly emphasized.

The classroom size was 35 in this school, except that conversation and grammar drill classes had 20 students. Double desks are bolted to the floor. This high school is used for adult classes from 5:00-9:00 p.m. in the evening. Four hundred adults (with instruction in Romanian, not English) are finishing their high school education. They can choose to take examinations for other occupations or to go to the university when they finish high school.

We talked with personnel at the Training Institute for Gerontology at Bucharest, which had three divisions concerned with 1) clinical assistance, 2) experimental studies, and 3) social gerontology of the aging. I was told that all districts have geriatric consulting rooms for medical assistance with about 100 such now. The plan is to have 500 in five years, so evidently the need for more is recognized. Both medical and social nurses are trained to work with the elderly. They have care-houses for those basically able to manage and hospital-type facilities for the chronically ill or disabled. I did not visit any of these. They attempt to have the care-houses seem like homes rather than hospitals, we were told, and people in these homes in their seventies frequently marry.

INFLUENCE OF DIETARY TRANS-FATTY ACIDS ON SWINE LIPOPROTEIN COMPOSITION AND STRUCTURE

(By Richard L. Jackson, Joel D. Morrisett,¹ Henry J. Pownall,¹ Antonio M. Fotto, Jr.,¹ Okinori Kamio,² Hideshige Imai,² Richard Tracy,³ and Fred A. Kummerow⁴)

Abstract. Four groups of 20 weanling swine each were fed either (a) basal diet, (b) basal plus hydrogenated fat (13 percent *trans*), (c) basal plus hydrogenated fat (13 percent *trans*) and 0.4 percent cholesterol, or (d) basal plus beef tallow (all *cis*). After six months of feeding, the animals were killed and the blood and aortas were removed. Very low density, low density, and high density lipoproteins were then isolated from the plasma by ultracentrifugal flotation. Although the fatty and composition of the basal diet was different from the diets supplemented with either hydrogenated fat containing *trans*-fatty acid or beef tallow containing all *cis*, the lipid and fatty acid or compositions of each of the isolated lipoprotein classes for the four groups of animals were remarkably similar. Elaidate was clearly incorporated into the lipoproteins of animals fed hydrogenated fat, but the level of incorporation was generally less than 5 percent. In a direct comparison of the structure of the lipoproteins from the different groups, we did not find any significant differences in their physical properties as determined by pyrene fluorescence and electron paramagnetic resonance methods. Grossly visible fatty streaks and fibrous plaques were not found in any of the swine aorta. However, light and electron microscopy indicated the presence of atherosclerotic lesions in the distal abdominal aorta and bifurcation. These studies demonstrate that a diet containing a substantial amount of *trans*-fatty acid leads to a small but definite incorporation into the swine lipoproteins. However, such changes had relatively little effect on lipoprotein structure or the presence of atherosclerotic lesions in these 6-month-old swine.

A diet containing both a high percentage of saturated fat and cholesterol has commonly been used to produce atherosclerosis in various animal models [1-6]. In many of these studies, the saturated fats were obtained from commercial hydrogenation of vegetable shortenings and oils. Because of the occurrence of *trans*-fatty acids (claidic acid) in these fats, the animal studies have raised an important question of the atherogenicity to man of certain hydrogenated vegetable fats. Although it is well documented that dietary *trans*-fatty acids are incorporated into serum lipids and tissues [7-10], fragmentary information is available on their effect on the chemical and physical properties of the isolated lipoprotein fractions. The present study was designed to determine these effects using two different types of dietary

Abbreviations: VLDL, very low density lipoproteins ($d < 1.006$); LDL, low density lipoproteins ($d 1.020-1.060$); HDL, high density lipoproteins ($d 1.000-1.210$); GLC, gas-liquid chromatography; TLC, thin-layer chromatography; EPR, electron paramagnetic resonance; FA, fatty acid; TEMPO, 2,2,6,6-tetramethylpiperidine-1-oxyl.

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saturated fat. In addition, the degree of atherosclerosis was determined by gross inspection after Sudan staining and with the aid of light and electron microscopy. Groups of 20 (each) weanling swine were fed for 6 months either hydrogenated fat containing *trans*-fat or beef tallow containing only *cis*-fat. Since high cholesterol feeding (1-2 percent) is known [2, 3] to induce both hyperlipidemia and atherosclerosis in pigs, we avoided this complicating factor to more precisely delineate the effect of a diet rich in *trans*-fatty acids. This baseline information concerning the effects of a high *trans*-fatty acid diet as distinct from a hypercholesterolemic diet on the plasma lipids and lipoproteins may be of value to others who attempt to assess the dietary contributors to atherogenicity using the pig as a model system.

MATERIALS AND METHODS

Animals and diets

Eighty purebred Yorkshire barrow piglets were maintained in an air-conditioned facility equipped with a slotted concrete floor and self-feeding and self-watering devices. The swine were divided into four groups and were fed the diets shown in Table 1. The total fatty acid composition of each diet is given in Table 2. The overall P/S ratios of the basal diet, basal plus hydrogenated fat, and basal plus tallow were 2.90, 0.55, and 0.34, respectively. The basal diet that contained 3 percent fat and furnished the equivalent of 14.3 percent protein was composed of 1,745 pounds ground corn, 200 pounds defatted soybean meal, and 55 pounds of a lysine, multiple vitamin, and mineral premix/ton of basal ration [11]. The cholesterol content of all diets, with the exception of group 1, was less than 0.01 percent. All piglets were fed the indicated diets from approximately 8 weeks of age until they were slaughtered at 6 months. The average initial weight was 42 pounds and the final weight was 230 pounds. When the animals reached approximately 230 pounds, they were fasted for 12 hr and slaughtered in groups of 20 each. The blood from each animal was collected in EDTA and sodium azide to give final concentrations of 0.01 percent and 0.001 percent, respectively; the cells were removed by low-speed centrifugation and the plasma was stored at 4°C for subsequent lipoprotein isolation.

TABLE 1.—COMPOSITION OF SWINE DIETS

	Stock ¹ (pounds)	Used fat ² (pounds)	Hydrogenated fat ³ (pounds)	Beef tallow ⁴ (pounds)	Cholesterol ⁵ (grams)
Group:					
1.....	100	10	3.....		200
2.....	100	10	3.....		0
3.....	100			13	0
4.....	100				0

¹ Stock diet contained 1,745 lb of ground yellow corn, 200 lb defatted soybean meal and 55 lb of a lysine, multiple vitamin and mineral mix. The mix consisted of 5 percent lysine, 20 percent calcium, 9 percent phosphorous, 15 percent sodium and potassium chloride, 0.004 percent calcium iodate, 0.018 percent zinc, 0.18 percent iron, 0.14 percent manganese as oxides or carbonates, and the following vitamins per pound: 40 mg riboflavin, 100 mg d-pantothenic acid, 300 mg niacin, 2,000 mg choline, 0.32 ug vitamin B₁₂, a minimum of 60,000 USP units of vitamin A palmitate, 60,000 IU of vitamin D₃, and 165 IU of vitamin F. (11, 12).

² Discarded hydrogenated soybean oil obtained from a local deep fat frying operation.

³ Fan fry (Courtesy of Swift & Co., Chicago, Ill.)

⁴ Courtesy of Oscar Meyer & Co., Madison, Wisc.

⁵ The crystalline cholesterol was dissolved in the used fat.

TABLE 2.—FATTY ACID COMPOSITION OF DIETS¹

Fatty acid: ²	Basal	Basal and used hydro- genated fat	Basal and beef tallow
12:0		0.4	
14:0	0.2	1.5	3.1
14:1			1.0
16:0	16.1	19.1	24.5
16:1	.9	.9	3.1
17:0	.9	.2	.8
16:2	1.7		1.2
18:0	2.3	8.6	15.1
18:1 cis	23.1	39.8	37.7
18:1 trans	.5	13.0	.5
18:2	53.0	15.8	12.3
18:3	1.8	.7	.4
20:1			.8

¹ Weight percent of total fatty acids. Each value is mean of at least 2 individual determinations.

² Number of carbon atoms: number of double bonds.

Preparation of tissue

The aorta was removed as soon as possible and processed for Sudan staining or for light and electron microscopy. For Sudan staining, the aorta was opened longitudinally along the anterior wall, flattened and fixed in formalin, stained for lipid with Sudan IV, stored in sealed plastic bags [13], and shipped to New Orleans for grading. For light and electron microscopy, the aorta was fixed by immersion in 4 percent glutaraldehyde in 0.1 M Sorensen's phosphate buffer pH 7.4. For light microscopy, six evenly spaced cross sections were cut from the abdominal aorta from the diaphragm through the trifurcation and were stained with hematoxylin-erosion, periodic acid-Schiff, Weigert elastica, or Sudan III. Specimens for electron microscopy were obtained from the distal abdominal aorta. They were post-fixed in buffered 1 percent osenic acid for 2 hr, dehydrated with alcohol, embedded in epoxy resin, sectioned with a Porter Blum MT-1, and double stained with uranyl acetate and lead citrate. The frequency of degenerated smooth muscle cells in 3-6 embedded blocks was counted at 5,000 or 9,000 \times magnification and the results were compared [14].

Isolation of lipoproteins

Each of the lipoprotein classes was isolated from a pool of the plasma within each group of animals. The lipoproteins were isolated by the ultracentrifugal flotation procedure described previously [15, 16]. A Beckman Model L2-65 centrifuge (Spineo Div., Palo Alto, CA) equipped with a 60 Ti rotor was operated at 8°C and 55,000 rpm. The density ranges for the isolation of the lipoproteins were as follows: VLDL, $d < 1.006$; LDL, $d \ 1.202-1.060$; and HDL, $d \ 1.090-1.210$. The density fraction between 1.060-1.090 was not studied since it was shown previously that it contained both LDL₂ and HDL [16]. In general, this density range (LDL₂) accounted for less than 10 percent of the plasma lipid. Each of the lipoproteins was refloated twice at its highest density. By immuno-chemical techniques, VLDL and LDL reacted with antisera prepared to pig apoB, but not to the major HDL protein, apoA-I; HDL gave procipitin lines only to anti-apoA-I. None of the lipoproteins reacted with anti-pig albumin. The isolated lipoproteins were extensively dialyzed against 0.9 percent NaCl, 0.01

percent EDTA, 0.001 percent sodium azide pH 7.4. In some of the studies, the samples were concentrated to about 30 mg/ml in a colloid bag (Schleicher and Schuell, Keene, NH).

Lipid determination

Plasma cholesterol and triglyceride were determined by automated methods [17]. Total lipids from each lipoprotein class were extracted with chloroform-methanol 2:1 by the method of Folch, Lees, and Sloane Stanley [18]. Lipid extracts were diluted to known volumes and aliquots from each sample were taken for determination of the total weight. Separation of lipid classes was performed by preparative thin-layer chromatography (TLC) on silica gel G as described previously [19, 20]. Free and esterified cholesterol were determined on appropriate aliquots of the isolated lipids by the method of Sobel and Fernandez [21], phospholipid phosphorus by the method of Bartlett [22], and triglycerides by gravimetric methods [20]. The fatty acid composition of the methyl esters of the appropriate lipid class was determined by gas-liquid chromatography (GLC) using a Barber-Coleman (Rockford, IL) Model 5000 gas chromatograph as described previously [19, 20]. The instrument was equipped with a 1.8 m U-shaped glass column, 3.2 mm ID, containing ethylene glycol succinate polyester, 15 percent on Chromosorb W AW, 80-100 mesh.

The percentages of methyl oleate (C 18:1 *cis*) and methyl elaidate (C 18:1 *trans*) were determined by capillary GLC [23] (hexadecanoate was used as an internal standard) or by infrared spectrophotometry with the aid of a Beckman IR-7 spectrometer equipped with a beam condenser and sodium chloride ultra-microcavity liquid cells. A 10-percent concentration of samples of methyl esters and standard mixtures of methyl oleate and methylelaidate from 5, 10, 20, 30, and 40 percent in CS₂ were read and quantified by triangulation and read from a standard curve [24].

Pyrene-fluorescence studies

Lipoproteins were labeled by a modification of a previously described method [25]. Typically, 0.025 ml of an ethanolic solution of pyrene (20 mg/ml) was thoroughly mixed (vortex mixer) with 5 ml of 0.05 M Tris-HCl pH 7.4. One ml of the resulting fine mixture was then added to 1 ml of lipoprotein (2 mg protein/ml and gently agitated). The excimer/monomer fluorescence ratios were determined using an Aminco Bowman spectrofluorimeter (American Instrument Co., Silver Spring, MD) that was equipped with a thermostated cell compartment. The instrumental parameters and methods for data calculation were identical to those described by Soutar et al. [26].

Electron paramagnetic resonance (EPR) studies

To determine the effect of diet on the fluidity of the lipoprotein particle, we have used the paramagnetic compound 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and have measured its thermotropic properties by EPR [27, 28]. TEMPO was prepared by the method of Rozantsev [29]. To each lipoprotein (30 mg/ml) was added 5 μ l of an aqueous solution of 2.33 mM TEMPO. The mixtures were then transferred to Corning micropipettes and the EPR spectra were recorded on a Varian E-12 spectrometer (Varian Assoc., Palo Alto, CA) operated at a microwave frequency of 9.15 GHz. The temperature of

the microwave cavity was regulated by a Varian variable temperature controller and was measured by a Tri-R electronic thermometer (Tri-R Instruments, Rockville Center, NY) to an accuracy of $\pm 0.5^\circ\text{C}$. Samples were measured at 3°C intervals from 0 – 69°C after equilibration of the sample for 5 min. By this procedure, none of the lipoproteins studied appeared to undergo irreversible denaturation in the temperature range studied.

The fluidity parameter f defined by the equation

$$f = \frac{H}{H + P}$$

was determined from the relative amplitudes of the polar (P) and hydrophobic (H) components of the high-field resonance line (Fig. 2) [27, 28]. The value of f at each temperature was computed by digitization of the polar and hydrophobic spectral component amplitudes with a Hewlett-Packard (Palo Alto, CA) calculator model 91000-B equipped with a 9107-A digitizer. An XY plotter was used to plot these values against temperature.

RESULTS

Plasma lipid composition

Plasma lipid levels in the four groups of animals are presented in Table 3. At the low concentration of cholesterol used in the diet (0.4 percent), there were only small differences in the plasma cholesterol concentration in the animals fed hydrogenated fat plus or minus cholesterol (compare groups 1 and 2). The same general trend was true for the plasma triglyceride levels. Lipoprotein electrophoresis patterns of each from the four groups failed to reveal any differences; each showed characteristics α - and β -migrating bands. In addition, the ultracentrifugal flotation distributions of each plasma were identical. Based on these two techniques, there was no indication of a B-VLDL or HDL_c, which are present in swine fed 1.5 percent cholesterol [30].

Lipid and fatty acid composition of lipoprotein fractions

The lipid composition of isolated CLDL, LDL₁, and HDL for each diet group are given in Table 4. With the exception of minor differences, the lipid compositions of each lipoprotein class were all within reasonable agreement. To determine if the different diets were associated with changes in the FA spectra, the lipid fractions were methylated and the methyl esters were analyzed by GLC. As shown in Table 5, approximately 50 percent of the VLDL triglyceride FA was 18:0 and 18:1. The major saturated FA was 16:0. In general, there were no discernable differences in the FA composition of VLDL triglycerides in the four diet groups. The FA spectra of LDL cholesteryl esters and phospholipids were also similar for each diet. Approximately 75 percent of all the LDL₁ cholesteryl esters were oleic acid and linoleic acid. In contrast, the major fatty acids (50 percent) of the LDL₁ phospholipids were palmitic and stearic acids. The FA compositions of the HDL cholesteryl esters and phospholipids were nearly identical to those found in LDL₁ and, again, the variations between each diet group were only minor.

No detectable amounts of C 18:1 *trans*-FA (elaidate) were found in any of the lipoproteins from the basal diet (group 4) or the *cis* beef tallow diet (group 3). Elaidate was clearly incorporated into the lipoproteins of animals fed used fat and hydrogenated soybean oil (groups 1 and 2). However, the amount of elaidate was usually less than 5 percent of the total (except HDL cholesteryl esters) and considerably less than the *trans*-fatty acid composition of the diet; the HDL cholesteryl esters contained 10 percent elaidate.

TABLE 3.—PLASMA-LIPID COMPOSITION¹

	Plasma triglyceride	Plasma cholesterol	VLDL cholesterol	LDL cholesterol	HDL cholesterol
Group: ²					
1.....	70	149	17	91	41
2.....	41	124	11	66	47
3.....	25	119	5	71	43
4.....	46	99	5	64	36

¹ Lipid values are expressed as mg/100 ml and are the analyses of pooled blood from 20 swine per group.

² Diets described in table 1.

TABLE 4.—PERCENT DISTRIBUTION OF LIPIDS IN ISOLATED LIPOPROTEIN FRACTIONS

Lipoprotein fraction and group	Triglycerides	Phospholipids	Cholesterol	Cholesteryl esters
VLDL d<1.006:				
1.....	83.5	4.4	6.4	5.7
2.....	84.2	6.5	4.5	4.8
3.....	86.1	6.5	4.3	3.1
4.....	83.1	9.2	3.9	3.6
LDL ₁ d 1.010-1.060:				
1.....	6.0	22.5	13.9	57.6
2.....	8.0	19.2	14.4	58.3
3.....	11.2	25.9	14.9	48.0
4.....	10.4	16.9	14.0	58.7
HDL d 1.090-1.210:				
1.....	1.7	25.4	6.5	66.3
2.....	1.5	26.8	5.6	66.1
3.....	1.3	25.0	4.8	68.9
4.....	2.5	25.7	6.7	65.1

Pyrene fluorescence studies

As shown previously [25, 26, 31], the pyrene excimer/monomer (E/M) ratio provides a sensitive measure of changes in the viscosity of the hydrocarbon core of lipoproteins. Therefore, the E/M ratios of pyrene-labeled LDL₁ and HDL from groups 1-4 were measured as a function of temperature (Fig. 1). In each instance, an increase in temperature caused an increase in the E/M value except at higher temperatures, where thermal dissociation of the excimer form is competitive with excimer fluorescence. Regardless of the diet, there was little change in the E/M versus temperature for each lipoprotein class.

EPR studies

TEMPO distributes between the bulk aqueous phase and the fluid-lipid phase of a lipoprotein particle (Fig. 2). The EPR spectrum of TEMPO in such a system normally exhibits three sharp, equally spaced, hyperfine lines. The high-field hyperfine line is split into two components, the lower field of which originates from TEMPO in the hydrophobic environment and the higher field, which is due to

TEMPO in the polar aqueous environment. As the temperature of this system is increased, more lipoprotein lipid becomes fluid, resulting in a greater distribution of TEMPO into the hydrophobic phase and producing an increase in the amplitude of the hydrophobic component and a decrease in the amplitude of the polar component. The ratio of the hydrophobic spectral component to the sum of the hydrophobic plus polar components can be used to calculate a relative fluidity parameter, f , for lipoprotein lipids.

TABLE 5.—FATTY ACID COMPOSITION OF VERY LOW DENSITY LIPOPROTEIN TRICLYCERIDES, LOW DENSITY LIPOPROTEIN PHOSPHOLIPIDS AND CHOLESTERYL ESTERS, AND HIGH DENSITY LIPOPROTEIN PHOSPHOLIPIDS AND CHOLESTERYL ESTERS¹

		Fatty Acids				
		16:0	18:0	18:1 (n-9)		18:2 (n-6)
				Cis	Trans	
Very low density lipoprotein:						
Triglycerides:						
Group 1.....	28.6	6.6	38.3	3.0	94.4	
Group 2.....	31.2	6.7	37.5	3.5	13.4	
Group 3.....	32.5	8.1	34.5	-----	18.2	
Group 4.....	33.3	6.4	31.8	-----	32.2	
Low density lipoprotein:						
Phospholipids:						
Group 1.....	24.8	23.1	17.9	2.8	18.8	
Group 2.....	22.1	24.0	17.9	3.7	19.5	
Group 3.....	20.8	26.2	20.0	-----	17.7	
Group 4.....	24.3	26.0	18.5	-----	17.0	
Cholesteryl esters:						
Group 1.....	10.3	2.4	² 28.3	(³)	48.0	
Group 2.....	10.8	1.9	² 28.0	(³)	48.0	
Group 3.....	11.5	2.1	28.0	-----	47.1	
Group 4.....	10.5	3.3	27.5	-----	45.7	
High density lipoprotein:						
Phospholipids:						
Group 1.....	17.8	24.0	24.1	5.5	20.2	
Group 2.....	17.8	24.9	24.1	(³)	17.7	
Group 3.....	17.2	27.2	19.3	-----	16.6	
Group 4.....	16.3	24.6	18.7	-----	14.6	
Cholesteryl esters:						
Group 1.....	11.5	1.1	² 27.7	(³)	51.5	
Group 2.....	12.2	.8	19.2	10.0	47.1	
Group 3.....	19.6	.9	29.1	-----	41.2	
Group 4.....	13.0	.9	31.1	-----	40.5	

¹ Expressed as percent of total. For clarity, the minor FA constituents were not listed.

² Cis plus trans.

³ Insufficient material.

Plots of f versus temperature for groups 1–3 are shown in Fig. 3 for VLDL, LDL₁, and HDL. For VLDL, the curve is initially a straight line and begins to reach a limiting value of about 0.3 at 33°C. For LDL₁, the curve is somewhat sigmoidal, exhibiting a sharp increase in fluidity in the range 27–33°C. After this sharp increase, the fluidity of LDL continues to increase linearly up to 69°C. This behavior is unlike that of VLDL in which the fluidity plateaus at about 33–36°C. Transition curves for HDL are also sigmoidal in shape. However, the change in fluidity in the range 24–36°C is not nearly so abrupt as that in LDL₁. This difference may be a reflection of the significantly greater amount of protein present in HDL that can serve to more effectively immobilize the lipids. Arrhenius plots of the data shown in Fig. 3 are presented in Fig. 4. For VLDL, two abrupt changes in slope are observed. For the lower transition, T_1 , this occurs at 27.5–32.0°C and for the higher transition, T_2 , it occurs at 41–44°C. For LDL₁, three abrupt changes in slope of the Arrhenius plots are observed. The lowest of these occurs at 26–27°C, the central transition at 31–33°C, and the

upper transition (T_3) at 58.5–61.0°C. For HDL, only two abrupt changes in slope are observed, the lower of these (T_1) occurring at 16.0–26.5°C and the higher (T_2) at 41–49°C. Tabulation of the transition temperature data for each of the lipoprotein classes from each diet group is given in Table 6. The close similarity in the transition temperature of each diet indicates that each lipoprotein class has similar thermotropic properties consistent with its lipid composition.

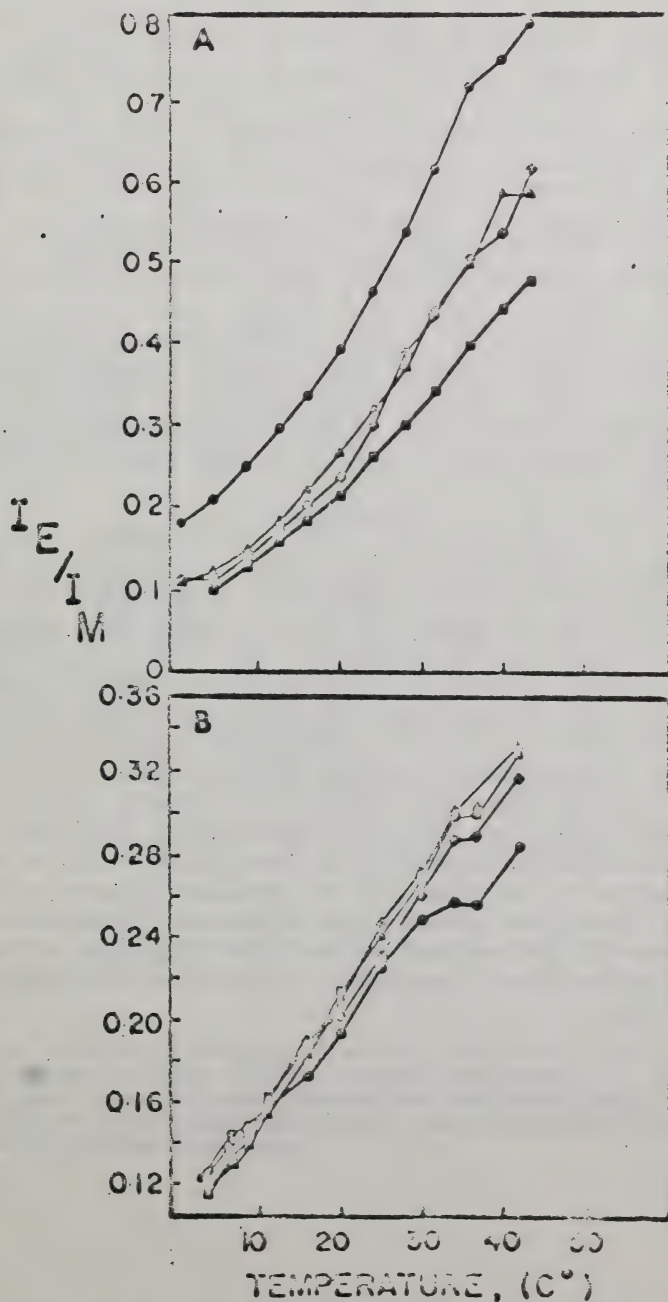


FIGURE 1.—Plots of pyrene excimer-monomer fluorescence intensity ratios (I_E/I_M) vs. temperature for HDL (A) and LDL (B). Group 1, circles; group 2, triangles; group 3, diamonds; and group 4, rectangles.

Changes in the aorta

Grossly visible, whitish, slightly elevated lesions, which were mostly in the distal abdominal aorta and trifurcation area, were infrequently observed in the freshly excised aorta from all groups at 6 months of age. No gross lesions were present in the proximal portions of the aorta from all groups. The abdominal aorta contained slightly more superficial Sudan IV-stained areas than the thoracic aorta (Table 7). However, no statistically significant differences were noted in the visible Sudan IV-stained areas between the aortas from swine fed animal fat, vegetable fat, or cholesterol. No advanced atherosclerotic lesions were observed in any group at 6 months of age. Under light microscopy, elevated lesions had collections of cells and extracellular materials. Superficial lard deposits and foam cells were sparse. In these areas, the internal elastica appeared broken or absent and, when stained with Sudan III, contained sudanophilic granules in the vicinity of the internal elastica and in the inner media. Portions of the aorta that appeared normal by light microscopy had, on electron microscopy, scattered degenerated smooth muscle cells and a small quantity of cell debris in the inner media. Grossly normal areas of the aortas from swine fed additional fat and cholesterol did not have a significantly higher frequency of degenerated smooth muscle cells than the grossly normal areas of the aorta from swine fed only the corn-soybean basal ration of 5.5 ± 0.18 percent and 5.1 ± 0.35 percent, respectively.

DISCUSSION

The plasma cholesterol concentrations of animals fed saturated fat and cholesterol were only slightly elevated compared to those of animals receiving the basal diet alone or basal plus saturated fat. Since the dietary sterol concentration was only 0.4 percent, we expected the plasma cholesterol values to be only slightly elevated. The major fatty acid of the basal diet was linoleic acid (53 percent). Compared to the basal diet lipoprotein FA, supplementing the diet with either hydrogenated vegetable fat or animal fat did not significantly alter the fatty acid compositions. Elaidic acid was present in the lipids from animals fed hydrogenated fat. With the exception of the cholesteryl esters of the HDL, however, they accounted for less than 5 percent of the total FA; the elaidate content of the HDL cholesteryl esters from Group 2 was 10 percent. The small incorporation of *trans*-FA did not lead to detectable differences in the thermotropic properties of each lipoprotein as determined by fluorescence and EPR methods.

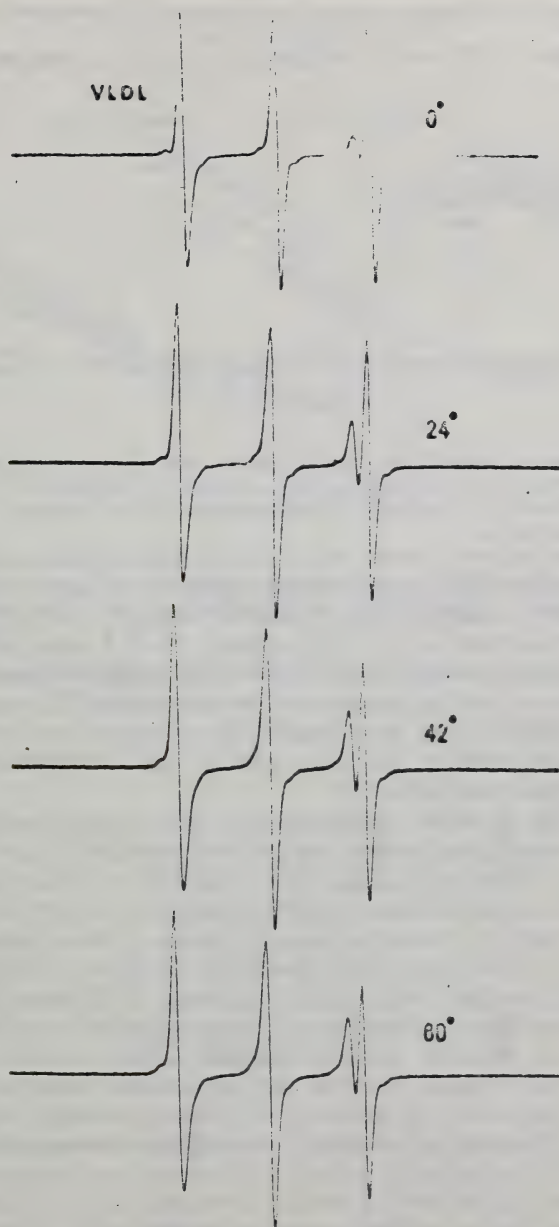


FIGURE 2.—Electron paramagnetic resonance spectrum of Tempo in the presence of a 30 mg/mi solution of VLDL isolated from group 1. As the hydrophobic lipid region of the lipoprotein becomes more fluid, more Tempo distributes into that fluid phase, resulting in an increase in the amplitude of the lowfield portion of the high-field resonance line.

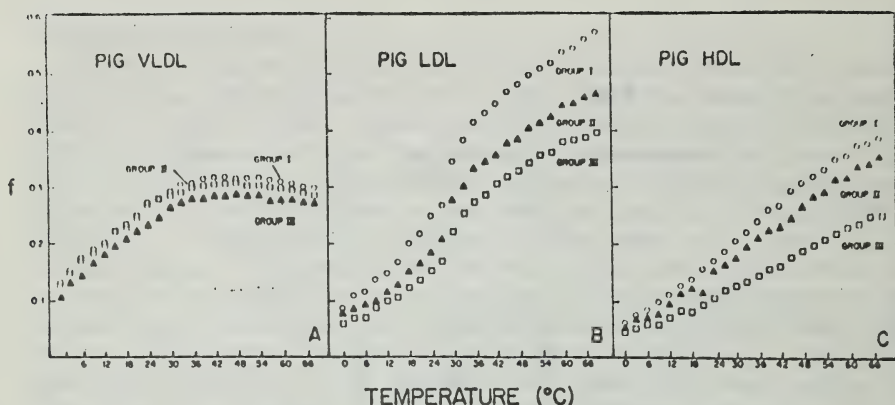


FIGURE 3.—Typical plots of the fluidity parameter, f , vs. temperature as determined with Tempo for pig VLDL, LDL, and HDL. Values of f were calculated from the hydrophobic and polar components of the high-field resonance line (illustrated in fig. 2).

In other studies [31] from this laboratory, it has been shown that these physical techniques can measure changes in the structure of lipoproteins. Morrisett et al. [31] altered the FA composition of diets that were highly unsaturated (P/S=4) or highly saturated (P/S=0.25). In contrast to the present swine study, the FA compositions of the human lipoproteins were markedly changed and resembled the dietary FA composition; the unsaturated diet lipoproteins were more fluid than the saturated ones.

The inability to show differences in the overall composition and structure of swine lipoproteins on the various diets may be due to the high content of linoleic acids, which may have swamped the effects of the *trans* fatty acids. However, swine required a high level of linoleic acid in their diet, so it was not possible to vary this factor [31]. Mattson et al. [33] have shown that the isomeric form of fatty acids in a hydrogenated fat that contained 34 percent 18:1 *trans* did not alter serum cholesterol or triglyceride in human subjects on a liquid formula diet, when fed with 20 percent linoleic acid. On the other hand, Vergroesen [34] found that, at an equivalent level of 34 percent elaidic acid, the serum cholesterol level was increased when either 10 or 24 percent linoleic acid was fed in a liquid formula diet to human subjects.

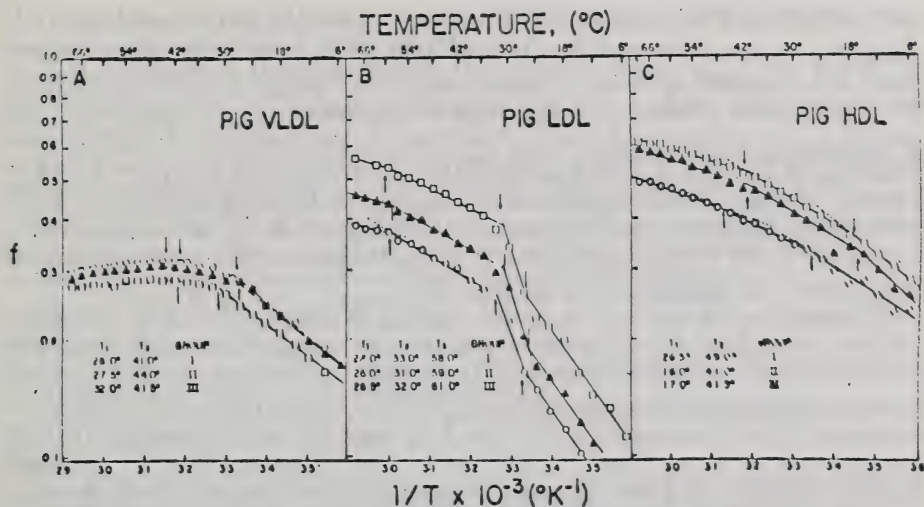


FIGURE 4.—Arrhenius plots of the fluidity parameter, f , for pig, VLDL, LDL₁, and HDL, isolated from the various groups. The temperatures at which these slope changes occur are a reflection of thermotropic changes of the constituent lipids.

TABLE 6.—TRANSITION TEMPERATURES FOR LIPOPROTEIN CLASSES (DETERMINED WITH TEMPO)

Lipoprotein class and group	Transition temperature		
	T ₁	T ₂	T ₃
VLDL:			
1	17	34	
2	28	44	
3	32	42	
4	26	42	
LDL ₁ :			
1	27	33	59
2	26	31	59
3	26	32	67
4	24	31	57
HDL:			
1	27	49	
2	16	41	
3	17	42	
4	28	52	

To date, the presence of Sudan IV-stainable fatty streaks and raised plaques has served as a convenient means of judging the extent of atherosclerosis [13]. The absence of Sudan IV-stainable fatty streaks at 6 months of age may be explained on the basis that atherosclerosis does not develop readily unless excessive amounts of fat and cholesterol are

present in the diet [35] and fed over an extended period of time [6]. In older swine, such visible signs of atherosclerosis were more apparent [32]. Higher levels of dietary fat and dietary cholesterol would probably have caused a more rapid accumulation of lipid and cell debris in the abdominal aorta. The diet of man contains a higher percentage of fat but a lower percentage of cholesterol than used in the present study. The 6-month-old swine on the fat and cholesterol supplemented diet consumed approximately 5 pounds of feed/day which, at a level of 0.4 percent cholesterol, is equivalent to the consumption of the amount of cholesterol in 40 eggs/day.

The subtle change in the aortic smooth muscle cell of the 6-month-old swine had no direct correlation to the composition and structure of serum lipoproteins. However, the presence of degenerated smooth muscle cells may reflect one of the first steps in the initiation of atherosclerosis. Time is required for the full expression of lesions. If this assumption is true, then inhibition of the degeneration of arterial smooth muscle cells would seem important for the control of the disease process. The present study indicated that the origin of dietary saturated fat, whether primarily of animal or vegetable origin, did not influence lipoprotein composition or structure when accompanied by a minimum level of dietary cholesterol.

TABLE 7.—INVOLVEMENT OF AORTA¹

	Thoracic aorta (Mean±SEM)	Abdominal aorta (Mean±SEM)
Group:		
1.....	0.42±0.12	2.17±0.98
2.....	.18±.03	1.32±.68
3.....	1.24±.69	3.22±.67
4.....	.44±.12	1.26±.77

¹ Percentage involved to normal area. No statistically significant differences between groups.

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Modification of In Vitro Rat Adrenal Corticosteroidogenesis by Dietary Fat¹

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ABSTRACT

Three groups of male weanling Holtzman rats were maintained, ad libitum, for 4 and 8 weeks on 1 of 3 diets: Purina Chow, hydrogenated soybean fat, and milk fat diets. The fats were added at the level of 36% total calories in the case of the hydrogenated soybean and milk fat diets. Adrenal homogenates prepared from tissues of each group of animals at the end of the dietary periods were used to measure the relative abilities to synthesize corticosteroids from endogenous substrates. Endogenous free cholesterol levels were found adequate to sustain the level of corticosteroids obtained. No concomitant cholesteryl ester hydrolysis was observed under the experimental conditions used. The adrenal synthetic ability for the three dietary groups was in the order milk fat > Purina Chow > hydrogenated milk fat. This order appeared not to be a reflection of the essential fatty acid status of the animals in the three dietary groups. The possible basis for this trend, and the implications of the findings for carbohydrate, protein, and lipid metabolism in the animal are indicated.

INTRODUCTION

In previous studies, we showed that the concentrations of rat adrenal-free and esterified cholesterol, as well as the fatty acid compositional pattern of the cholesteryl esters, were modified by feeding diets containing 10% and 20% partially hydrogenated soybean fat (1). Furthermore, the total ω -9 long chain fatty acids in the cholesteryl esters was significantly higher in these animals compared to animals fed similar diets but supplemented with 2% corn oil (1) or animals fed other linoleate-adequate fat diets (2).

In an attempt to find out how these modi-

fications might affect the cholesterol and cholesteryl ester-related functional activities of the adrenals, we measured the relative abilities of adrenal homogenates from rats fed 2 different fat diets—hydrogenated fat diet (HF) and milk fat (MF) for 4 and 8 weeks—to synthesize corticosteroids from endogenous substrates in vitro. Rats fed a regular ration of Purina Chow (PC) also were studied for purposes of comparison. The results of this investigation form the subject of this article.

MATERIALS AND METHODS

Male weanling Holtzman rats (15/dietary group), maintained, ad libitum, on 1 of the 3 diets, HF, PC, and MF, for 4 and 8 weeks were used in these experiments. The hydrogenated soybean fat and milk fat have been described previously (2) and were added to the basic fat-free stock (2) at the 18.6% level by wt (36% total calories) at the expense of sucrose. The

TABLE I
Fatty Acid Composition of the Dietary Fats^a

Fatty acid	Hydrogenated fat	Milk fat	Purina Chow ^b
wt % of total			
10:0	0.2	2.1	—
12:0	trace	4.6	—
14:0	0.2	8.3	2.2
14:1 ω 5	trace	4.4	—
16:0	8.1	23.3	19.8
16:1 ω 7	0.2	3.7	0.2
18:0	13.2	18.4	4.9
18:1 ω 9	76.5 ^c	30.6	31.8
18:2 ω 6	1.0 ^d	3.1	39.5
18:3 ω 3	trace	—	1.5
20:0	0.4	—	—
20:1 ω 9	0.2	1.4	0.3

^aEach value is the mean of three individual determinations. Fatty acids are designated by chain length: number of double bonds, the first located at the ω -position (from methyl end) indicated.

^bFat content 5.24% (Ralston Purina Company, Checkerboard Square, St. Louis, Mo.).

^cAverage *trans*, as elaidate, from IR and capillary gas liquid chromatographic analyses, is 48.4% of total fatty acids. The *trans*-unsaturation was found from previous degradative studies (1) to be essentially at the 9,10 position. Double bond designations of other unsaturated fatty acids based upon prior evidence (1,2).

^dMixture of octadecadienoates (1).

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mean body wt with standard errors (7 rats for each period of feeding) of the different dietary groups after the 4 week and 8 week feeding periods, respectively, were as follows: HF, 177.0 ± 7.3 ; MF, 197.0 ± 8.9 ; PC, 201.6 ± 6.6 and HF, 230.5 ± 10.8 ; MF, 269.2 ± 6.5 ; PC, 272.0 ± 6.8 . However, using Student's *t* test, these differences in body wt between groups were not significant, with the possible exception of HF group vs. PC group.

The fatty acid compositions of the fats present in the three diets are given in Table I. The MF diet had the most diverse fatty acid profile (chain length C_{10} - C_{20}), followed, in that order, by the PC and HF diets. The major fatty acids common to the three dietary fats were 16:0, 18:0, and 18:1. The 18:1 fraction in the HF diet was found to consist of 26.0% as oleate and 48.5% as the *trans*-isomer, elaidate. The lipids of the PC diet had a high content of linoleate (39.5%). The MF lipids had an adequate level of linoleate (3.1%) to meet the minimum essential fatty acid (EFA) requirements. The level of 1% 18:2 in the HF diet represents a mixture of isomers (1).

Fat-trimmed adrenals pooled from 6-7 animals were used. There was little variation in the average wt of the adrenal, irrespective of the dietary group (24.5-27.5 mg/adrenal). Each adrenal in the pool was cut in half before preincubation for 1 hr at 37 C, as described by Koritz and Peron (3,4), except that the preincubation medium was 50 ml 0.154 M NaCl solution containing 40 μ moles NaHCO_3 and 8.5 μ moles glucose/ml, adjusted to the optimum pH of 7.35 (4) with 1-2 drops of 1 N HCl. Preincubation has been found necessary for effective steroid production *in vitro* in response to exogenous adrenocorticotropin (ACTH) (5). Its use in these experiments ensured that any possible effects due to ACTH responses to the dietary treatments would not complicate the results.

Following the preincubation, homogenization was done in 6.2 ml solution (pH 7.35) containing 2.0 μ moles NaCHO_3 and 1.6 μ moles Ca^{++} /ml 0.154 M KCl. The amounts of corticosteroids released into the preincubation medium were determined as described below and were found to be small in all cases (1.5-2.0 μ g/100 mg adrenal tissue).

For the incubation, each tube contained 1.0 ml adrenal homogenate and 1.0 ml incubation medium—0.154 M KCl solution containing 5.4 μ moles glucose-6-phosphate and 2.2 μ moles nicotinamide adenine dinucleotide (NADP) or, in place of these two components, 2.2 μ moles NADPH/ml 0.154 M KCl. Blank (control) tubes contained 1.0 ml heat-denatured homogenate.

The total volume/tube was 2.0 ml, with a depth of ca. 1 cm. The incubation was for 1 hr at 38 C (in a metabolic shaker), after saturation of the medium with 95% O_2 -5% CO_2 gas mixture and capping the tubes. The incubation was terminated by adding 3.0 ml chloroform-methanol, 2:1 (v/v). Protein was determined routinely by the biuret method (6).

The total lipids were extracted at the end of the incubation, first with 3.0 ml aliquots of chloroform-methanol, 2:1 (v/v) and then with 3.0 ml aliquots of methylene chloride, 2 times in each case. The combined extracts for each tube were reduced to dryness under nitrogen and the residue dissolved in 0.5 ml methylene chloride for storage. The total lipids were fractionated by thin layer chromatography (TLC) (1) against known standards (cholesteryl esters, triglycerides, free fatty acids, cholesterol, and corticosterone). The first solvent system used was chloroform-acetone, 80:20 (v/v), after which the solvent front region (R_f 0.80-0.95) was scraped off. Lipids were recovered from the scrapings by elution with chloroform-ether, 1:1 (v/v), and then were fractionated into classes by TLC using a second solvent system, high boiling petroleum ether-diethyl ether-glacial acetic acid, 80:20:1 (v/v). The cholesteryl esters, triglycerides, and free fatty acids were recovered separately by the usual procedure (1). The rest of the TLC plate from the development in the chloroform-acetone system was exposed momentarily to iodine vapor. The corticosterone band (R_f 0.23), cholesterol band (R_f 0.54), and two plain R_f regions below (R_f 0.10-0.15) and above (R_f 0.30-0.35) the corticosterone band were scraped off and the lipids eluted once with chloroform-methanol, 2:1 (v/v) and two times with methylene chloride. The combined extracts were taken to dryness under nitrogen and the lipid material redissolved in methylene chloride.

Cholesterol and cholesteryl ester contents of the adrenals were determined routinely by the colorimetric method of Sobez and Fernandez (7). Quantification of the cholesteryl esters was done by gas liquid chromatography, as described by Walker and Carney (8). Corticosterone and lipid materials recovered from the two plain R_f regions were determined colorimetrically after reaction with 2,5-diphenyl-3-(4-styrylphenyl)-tetrazolium-chloride (K & K Laboratories, Plainview, N.Y.)—an approach commonly referred to as the blue tetrazolium (BT) procedure, first described by Elliott and coworkers (9). The reagents were scaled up to a final volume of 5.0 ml. The final yellowish-reddish color was read at 510 nm (Bausch and

TABLE II
In Vitro Corticosteroid Synthesis from Rat Adrenal Endogenous Precursors^a

Dietary group	$\mu\text{g}/100 \text{ mg wet tissue}^b$	
	Fed for 4 weeks	Fed for 8 weeks
Hydrogenated fat	7.3 (6.8- 7.8) ^c	6.0 (4.7- 7.2)
Purina Chow	12.5 (11.2-14.7)	10.1 (9.5-11.3)
Milk fat	26.3 (24.4-29.9)	20.2 (20.0-20.7)

^aEach value is the mean net synthesis from 3 experiments, with 5-6 incubation tubes/experiment. A pool of adrenals from 6-7 animals was used/experiment.

^bNet new synthesis = total corticosteroid (blue tetrazolium positive) determined after incubation minus the control (heat denatured homogenate) value. Control values: hydrogenated fat, 1.7; Purina Chow, 2.3; milk fat, 2.0 $\mu\text{g}/100 \text{ mg wet tissue}$.

^cRange of values from three experiments are in parentheses.

Lomb Spectronic 20) and the steroid concentration obtained from a standard curve prepared with corticosterone (Applied Science Labs., State College, Pa.). The combined steroid levels determined in the extracts from the two plain R_f regions were designated as the non-corticosterone steroids (non-CCS). All corticosteroid concentrations were expressed as $\mu\text{g}/100 \text{ mg wet adrenal tissue}$.

RESULTS

The extent of production of corticosteroids from endogenous precursors by rat adrenal homogenates from animals in the three dietary groups is shown in Table II. For the animals fed the HF diet for 4 and 8 weeks, the figures for the net new synthesis correspond, respectively, to ca. 4.3 times and 3.5 times the original endogenous level of corticosteroids in the adrenals (1.7 $\mu\text{g}/100 \text{ mg wet tissue}$). With respect to the animals fed the PC diet for 4 and 8 weeks, the values for the net synthesis were 5.4 times and 4.4 times, respectively, the original endogenous concentration of 2.3 $\mu\text{g}/100 \text{ mg wet}$

tissue. In the case of the animals fed the MF diet for 4 and 8 weeks, the corresponding values were 13.2 times and 10.1 times, respectively, the endogenous concentration of 2.0 $\mu\text{g}/100 \text{ mg wet tissue}$.

Corticosterone was found to be the predominant corticosteroid of the rat adrenals by the assay procedure employed here. However, the second predominant and, sometimes equally prevalent, steroid produced by the rat adrenal is 18-hydroxy-11-deoxycorticosterone (18-OH-DOC), which, because it exists in the 20,18-hemiketal form (10) is BT negative and so would not be detected. The production of this steroid is enhanced by ACTH stimulation. Since a preincubation step was used, it is doubtful that any significant amounts of this steroid would be produced during the incubation. With this caveat in mind, calculations based upon the data from the TLC analyses showed that corticosterone constituted 87.6%, 86.4%, and 88.7% of the total rat adrenal BT positive corticosteroids for the animals fed, respectively, the HF diet, the PC diet, and the MF diet. It was the major BT positive corticosteroid arising

TABLE III
Concentrations of Adrenal Cholesterol and Cholesteryl Esters^a

Compound ^c	Fed for 4 weeks ^b			Fed for 8 weeks		
	HF	PC	MF	HF	PC	MF
Cholesteryl esters (endogenous)	15.4 \pm 0.5	6.9 \pm 0.1	9.6 \pm 0.3	13.2 \pm 0.4	6.8 \pm 0.2	9.8 \pm 0.3
Cholesteryl esters (after incubation)	15.3 \pm 0.6	7.0 \pm 0.0	9.5 \pm 0.3	13.3 \pm 0.2	6.9 \pm 0.2	9.6 \pm 0.5
Cholesterol (endogenous)	1.2 \pm 0.0	2.0 \pm 0.1	2.4 \pm 0.1	1.3 \pm 0.2	1.4 \pm 0.1	2.5 \pm 0.2
Cholesterol (after incubation)	1.0 \pm 0.0	1.7 \pm 0.0	2.0 \pm 0.3	1.1 \pm 0.0	1.1 \pm 0.1	2.1 \pm 0.2

^aValues are the means of 3 separate analyses involving adrenals pooled from 6-7 rats.

^bHF = hydrogenated fat, PC = Purina Chow, and MF = milk fat.

^cGiven as mg/g wet adrenal tissue.

TABLE IV

Cholesteryl Ester Composition of Adrenals
from Rats Fed Different Fat Diets for 8 Weeks^a

Ester	Dietary groups, mole %		
	Hydrogenated fat	Purina Chow	Milk fat
12:0	---	---	1.9 (1.8- 2.0)
14:0	5.0 (3.8- 6.3)	3.7 (3.3- 4.2)	6.3 (6.1- 6.6)
14:1 ω 5	1.9 (1.6- 2.6)	0.5 (0.3- 0.8)	2.9 (2.7- 3.1)
16:0	10.5 (10.0-11.0)	9.9 (9.0-11.0)	10.9 (10.5-11.2)
16:1 ω 7	5.6 (4.5- 6.8)	2.6 (2.1- 3.1)	5.0 (5.0- 5.1)
18:0	3.4 (2.8- 4.1)	4.0 (3.1- 5.0)	6.1 (5.9- 6.4)
18:1 ω 9	37.3 (34.1-41.0)	12.3 (11.5-13.1)	23.5 (22.8-24.3)
18:2 ω 6	0.8 (0.6- 1.1)	6.8 (5.9- 7.8)	5.1 (4.9- 5.3)
20:1 ω 6	---	1.7 (1.0- 2.5)	1.2 (1.0- 1.4)
20:2 ω 6	2.7 ^c (2.0- 3.5)	1.0 (0.8- 1.3)	0.8 (0.8- 0.8)
20:3 ω 9	5.6 (5.0- 6.3)	0.3 (0.3- 0.3)	2.5 (2.3- 2.9)
20:3 ω 6	0.3 (0.3- 0.3)	0.5 (0.3- 0.8)	1.1 (1.0- 1.3)
20:4 ω 6	6.4 (5.6- 7.4)	8.1 (7.5- 8.7)	5.5 (5.4- 5.7)
22:1 ω 6	---	10.6 (9.5-11.7)	4.2 (4.0- 4.4)
22:2 ω 9	4.2 ^c (4.1- 4.5)	trace	3.6 (3.0- 4.2)
22:2 ω 6	trace	2.0 (1.6- 2.5)	trace
22:3 ω 9	3.4 (3.1- 3.8)	0.4 (0.3- 0.5)	2.0 (2.0- 2.0)
22:3 ω 6	trace	1.0 (0.6- 1.5)	2.0 (2.0- 2.1)
22:4 ω 6	4.3 (4.0- 4.7)	14.0 (13.1-15.0)	7.8 (7.3- 8.7)
22:5 ω 9	0.1 (0.1- 0.1)	1.3 (0.9- 1.4)	1.9 (1.2- 2.7)
22:5 ω 6	1.0 (0.7- 1.5)	7.9 (7.0- 8.9)	2.0 (1.5- 2.6)
22:5 ω 3	1.6 (0.8- 2.4)	---	---
22:6 ω 6	4.2 (4.0- 4.4)	10.9 (9.6-11.4)	3.0 (2.7- 3.4)
22:6 ω 3	1.3 (0.9- 1.5)	0.4 (0.3- 0.7)	trace

^aValues are the means of 3 separate analyses, as described in the text, with range of values in parentheses. The cholesteryl esters are designated by the fatty acid moiety chain length:number of double bonds, the first located at the ω -position (from methyl end of the molecule).

^bRepresent mixtures of isomers; their identities have been described (1).

from new synthesis.

The concentrations of adrenal free cholesterol and cholesteryl esters determined after the incubation for corticosteroid synthesis are presented in Table III. The cholesteryl ester concentrations before (endogenous levels) and after the incubation were found to be practically the same. With respect to the free cholesterol fractions, decreases, although small (ca. 15-21%), were observed in each case. The smallness of these decreases in comparison with some of the standard errors (Table III) raises doubts as to the significance of the differences between groups. Thus, although there is apparently a correlation between their respective quantitative values (expressed as $\mu\text{g}/100$ mg tissue) and the amount of corticosteroids synthesized during the incubation (Tables II and III), such a conclusion would be unwarranted on the basis of the data presented.

The fatty acid composition of the adrenal cholesteryl esters from the animals fed the different fat diets is shown in Table IV. The wide range of cholesteryl esters is obvious and is consistent with published work (1,8,11). The fatty acid compositions of the dietary fats

(Table I) seemed to be reflected, to some extent, in the levels of the different cholesteryl esters, especially up to cholesteryl linoleate. Dietary fat modification of the cholesteryl esters of the longer chain fatty acids (C_{20} - C_{22}) manifested itself in the differences in the relative amounts of the major cholesteryl esters (cholesteryl-20:3 ω 9, -20:4 ω 6, -22:1 ω 6, -22:4 ω 6, -22:3 ω 9, -22:5 ω 6, and -22:6 ω 6). These fatty acyl designations were based upon previous evidence (1,2). Furthermore, the sole occurrence of mixtures of cholesteryl-20:2 isomers, and of cholesteryl-22:2 isomers in the adrenals of the animals fed the HF diet seems noteworthy. Their identities have been published elsewhere (1).

DISCUSSION

Our results confirm previous findings by others that rat adrenal homogenates are capable of corticosteroid synthesis, *in vitro*, utilizing the endogenous free cholesterol present in the adrenals (12). More importantly, it was shown that the ability for corticosteroidogenesis was dependent upon the nature of the antecedent

dietary fat. This ability was found to be in the order MF > PC > HF. Following the incubation for steroidogenesis, the total cholesteryl ester concentration in the adrenal homogenate remained, in all cases, practically unchanged, indicating no net cholesteryl ester hydrolysis under the conditions of the incubation.

It has been suggested that EFA deficiency leads to a decreased ability of rat adrenals to synthesize corticosteroids (11,13). Although the HF diet was low in linoleate (18:2 ω 6), the growth pattern and physical well-being of the animals fed this diet compared well with the other two dietary groups. Over the relatively short feeding periods employed, no overt EFA deficiency symptoms were observed. Besides, the adrenals seem to have the ability to conserve and metabolize even minimal amounts of dietary linoleate (1,2), resulting in the synthesis of the long chain polyunsaturated fatty acids of the ω -6 family. Consequently, the characteristic adrenal cholesteryl esters of the C₂₀ and C₂₂ polyunsaturated fatty acids (ω -6 family) were observed in the adrenals, irrespective of the dietary fat (Table IV). However, a summation of these cholesteryl ester types for each dietary group revealed the order PC > MF > HF (ca. 55%, 29%, and 15% total, respectively), in agreement with the order of linoleate levels in the dietary fats (Table I). Furthermore, it may be noted that the PC diet, which definitely contained the highest level of linoleate (EFA), led to a lower corticosteroidogenesis than the MF diet, which had a lower EFA content. Therefore, our results were probably not influenced by the EFA status of the three groups of animals.

It is not clear from the results why the PC diet led to a lower synthetic ability than the MF diet. One can only suggest that the more complete, or better balanced, fatty acid profile of the milk fat noted earlier may have something to do with it. The conversion of cholesterol to corticosteroids involves the side chain cleavage enzymes and a series of hydroxylases. The rate limiting step in this series of complex enzymatic reactions is believed to be the conversion of cholesterol to pregnenolone, which is also the site of action of the stimulation or acceleration of adrenal steroidogenesis by Ca⁺⁺ (4) or cyclic adenosine 5'-monophosphate (3,14). That the adrenals from the animals fed the HF diet were the least effective may be related partly to the high levels of cholesteryl elaidate in the adrenals (19-22%) under the HF regimen (1) and partly to the relatively low level of total long chain characteristic, polyenoic cholesteryl esters of the ω -6 family in connection with the composition of

the lipoprotein components of the key enzymes. A decreased capacity of energy yielding processes, leading to a decreased adenosine 5'-triphosphate synthesis (15), also may be involved. However, the data in this article do not provide much evidence bearing on the possible mechanisms by which these fat diets could affect corticosteroidogenesis.

Adrenal corticosteroids are involved in carbohydrate, protein, and fat metabolism (16). Their involvement in lipid metabolism pertains to their inhibitory effect upon lipogenesis and their lipolytic action upon adipose tissue and especially the liver, resulting in lipid mobilization. If our finding that rat adrenal corticosteroid synthesis is modified by the nature of the dietary fat holds under *in vivo* conditions, this could have important implications for some key aspects of carbohydrate, protein, and lipid metabolism in the animal. This aspect of the study needs to be investigated.

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Effect of Dietary Fat on the Release Rate of Cholesterol from Swine Erythrocytes (38077)

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It has been shown that there is a rapid exchange of cholesterol between lipoprotein and erythrocytes (1-5) or between plasma and erythrocytes (5-7). Numerous reports have shown that the cholesterol content and fatty acid composition of plasma were altered by dietary fat. Furthermore, the fatty acid composition of the erythrocyte lipids was significantly influenced by the dietary fat (8-13). Since lipids are involved in the structure of the cell, it is possible that dietary factors may exert some influence on the function of erythrocyte membranes (13, 14). However, whether dietary fat influences the cholesterol exchange between plasma and erythrocytes is still unknown. The purpose of the present study was to evaluate: (1) the effect of dietary fat on the lipid composition of plasma and erythrocytes, and (2) the effect of dietary fat on the release rate of cholesterol from erythrocytes.

Materials and Methods. Six-month-old swine were divided into three groups of 12 each and fed different dietary fats for a period of 8 mo. The basal diet which contained 14.3% protein, 3.0% fat, and 72.7% carbohydrate was composed of ground yellow corn, solvent extracted soybean meal, and a mineral-vitamin premix. The corn oil group was fed the basal diet mixed with 17% corn oil; the hydrogenated fat group was fed the basal diet with 17% partially hydrogenated soybean oil which contained approximately 50% *trans* fatty acids (margarine base stock). Blood was obtained from the jugular vein by heparinized syringe. The plasma and erythrocytes were separated by centrifugation and the buffy coat was discarded. The erythrocytes were washed

three times with saline solution (0.9% NaCl). Total lipids from the plasma and erythrocytes were extracted by the Folch procedure (15) using chloroform-methanol (2:1, v/v). Free and esterified cholesterol were determined on appropriate aliquots of the total lipid extracts by the method of Searcy and Bergquist (16). The fatty acid composition of the lipid moiety of the plasma and erythrocytes was determined by means of gas liquid chromatography (17). *Trans* fatty acids were also measured quantitatively by infrared absorption spectrometry of their methyl esters (18).

In order to obtain [^3H]-cholesterol-labeled erythrocytes, equal volumes of plasma and erythrocytes were mixed and incubated with ^3H -1,2 α -cholesterol (0.2 $\mu\text{Ci/ml}$ blood) at 37°C in a metabolic shaker. The aqueous solution of cholesterol was prepared using Tween 80 according to the method of Meier *et al.* (19). After obtaining the [^3H]-cholesterol-labeled erythrocytes, these labeled erythrocytes were incubated with their own unlabeled plasma. Samples were withdrawn at each time interval and centrifuged to obtain plasma and erythrocytes. The erythrocytes were washed four times with cold saline solution (0.9% NaCl), the lipids extracted from both plasma and erythrocytes and the cholesterol content and its radioactivity determined. The release rate of cholesterol from the erythrocytes obtained from swine fed the different dietary fats were compared from the specific activity changes vs time.

Results. Both the free and esterified cholesterol content in the plasma were higher in those animals fed hydrogenated fat which

TABLE I. Effect of Dietary Fat on Cholesterol Content in Plasma and Erythrocytes.

Cholesterol content mg/100 ml	Corn oil	Basal	Hydrogenated fat
Plasma (total)	96 ± 5 ^a	99 ± 8	129 ± 7
Plasma (free)	23 ± 1	24 ± 2	36 ± 3
Plasma (esterified)	74 ± 6	75 ± 6	94 ± 4
Erythrocytes	121 ± 5	122 ± 7	119 ± 3

^a Mean for three samples ± SEM, each containing pooled blood from four swine.

contained *trans* fatty acids as compared to those either fed corn oil or the basal diet (Table I). However, the quantity of free cholesterol within the erythrocytes appeared to be constant regardless of the dietary fat. It is noteworthy that the cholesterol present in the erythrocytes was entirely in the unesterified form. The two different dietary fats stimulated considerable differences in the total fatty acid patterns of the plasma and erythrocyte lipids (Table II). Percentage of the 18:1 and 18:2 were changed most drastically in both the plasma and erythrocyte. The *trans* fatty acid content in the plasma from the swine fed hydrogenated fat were approximately 12% and was present mainly in the triglyceride and the cholesterol ester fractions. The amount of *trans*

fatty acids in plasma from the swine fed corn oil or the basal diet was negligible. The content of the *trans* fatty acids in the erythrocytes from the swine fed hydrogenated fat was about 2%, none was present in the erythrocytes from the swine fed corn oil or the basal diet.

Incubation of ³H-1,2α-cholesterol with whole blood resulted in a decrease in the specific activity of the free cholesterol in the plasma and the concomitant increase of specific activity of the erythrocyte cholesterol. However, the specific activity of plasma esterified cholesterol showed no change throughout the 8 hr incubation (Fig. 1). On the basis of these data, 4 hr incubations were carried out in subsequent experiments to obtain the [³H]-cholesterol-labeled erythrocytes. After obtaining the [³H]-cholesterol-labeled erythrocytes, they were incubated with their own unlabeled plasma. The data are indicated in Fig. 2. The specific activity of cholesterol in the erythrocytes decreased as the incubation time was increased, while the specific activity in the free and esterified cholesterol in the plasma increased. The free cholesterol of plasma readily exchanged with erythrocyte cholesterol. However, the esterified cholesterol exchange between erythrocytes and plasma was negligible. As the curve in Fig. 2 appears to be a first order reaction, the data which show the degree of equilibration between erythrocytes and plasma at each

TABLE II. Effect of Dietary Fat on Fatty Acid Composition in Plasma and Erythrocyte Lipids.^a

Fatty acid ^b	Plasma			Erythrocyte		
	Corn oil	Basal	Hydrogenated fat	Corn oil	Basal	Hydrogenated fat
14:0	0.3 ± 0.0 ^c	0.6 ± 0.1	0.6 ± 0.0	0.4 ± 0.1	1.3 ± 0.4	2.3 ± 1.9
16:0	17.2 ± 0.5	22.4 ± 1.6	17.8 ± 0.1	30.6 ± 0.8	35.5 ± 2.9	30.6 ± 0.6
16:1	1.5 ± 0.1	2.7 ± 0.1	2.8 ± 0.2	trace	trace	trace
18:0	12.7 ± 0.8	12.4 ± 0.3	11.4 ± 0.3	15.0 ± 0.3	12.9 ± 0.2	12.0 ± 0.7
18:1	14.3 ± 0.6	21.7 ± 0.6	35.0 ± 1.0	24.5 ± 0.1	26.6 ± 1.9	35.4 ± 1.1
18:2	47.0 ± 1.2	33.1 ± 0.5	26.6 ± 1.0	26.0 ± 1.0	19.6 ± 0.2	16.5 ± 0.6
20:4	7.0 ± 0.3	7.1 ± 0.3	5.7 ± 0.1	3.5 ± 0.2	4.2 ± 0.5	3.0 ± 0.5

^a Expressed as a percentage of the total fatty acids.

^b Numbers before and after colon represent carbon chain length and number of double bonds, respectively.

^c Mean for three samples ± SEM, each containing pooled blood from four swine.

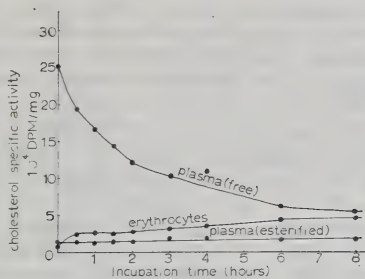


FIG. 1. Changes in specific activities of cholesterol in plasma and erythrocyte during incubation of $[^3\text{H}]$ -cholesterol with whole blood. Each point represents the average of three determinations.

time interval (Table III) can be plotted in exponential form. Plotting the degree of equilibration against incubation time on semilogarithmic graph paper was shown in Fig. 3. The release rate of labeled cholesterol from erythrocytes obtained from animals fed the different dietary fats can be compared. The calculated regression equations for equilibration between the erythrocytes and plasma from animals fed corn oil, basal and hydrogenated fat were $Y = 0.1574 + 0.2434x$, $Y = 0.1951 + 0.2286x$, and $Y = 0.1856 + 0.1518x$, respectively. The time required to reach 50% equilibration for the erythrocytes and plasma from

TABLE III. The Degree of Equilibration of $[^3\text{H}]$ -Cholesterol Between Erythrocytes and Plasma vs Time.

Time (hr)	Corn oil	Basal	Hydrogenated fat
1/2	1.94 ± 0.09^a	2.02 ± 0.09	1.76 ± 0.00
1	2.42 ± 0.07	2.69 ± 0.18	2.26 ± 0.06
2	4.53 ± 0.25	4.47 ± 0.46	3.14 ± 0.34
3	7.65 ± 1.07	7.60 ± 0.52	4.28 ± 0.35
4	—	—	6.22 ± 0.61

^a Mean for three samples \pm SEM. The degree of equilibration expressed as $a/(a - x)$, "a" being the final equilibrium specific activity for each experiment and "x" being the specific activity at time "t."

those fed corn oil, basal diet, and hydrogenated fat was; 1.24, 1.32, and 1.98 hr, respectively.

Discussion. The present data indicate that the plasma cholesterol level was increased in swine fed hydrogenated fat which contained *trans* fatty acids. This effect was consistent with a previous report (20) in which rats fed *trans* fatty acids had higher serum cholesterol levels than those fed the corresponding *cis* fatty acids. McMillan *et al.* (21) also found that feeding elaidinized oleic acid to rabbits caused a greater concentration of total, free, and esterified cholesterol in the serum than did the feeding of natural oleic acid. However, the reason for

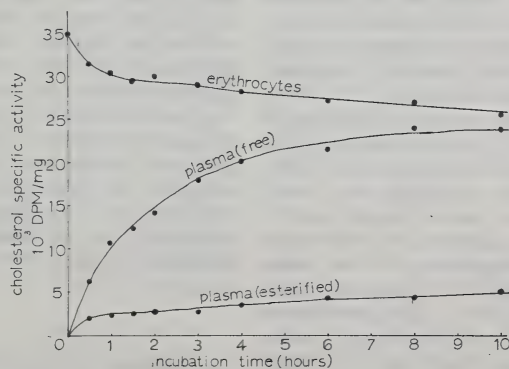


FIG. 2. Changes in specific activities of cholesterol in plasma and erythrocyte during incubation of $[^3\text{H}]$ -cholesterol labeled erythrocytes with unlabeled plasma. Each point represents the average of three determinations.

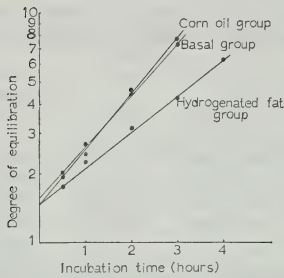


FIG. 3. The degree of equilibration of $[^3\text{H}]$ -cholesterol between erythrocytes and plasma expressed as $\log a/a-x$ vs time. Each point represents the average of three samples for each time interval.

increasing plasma cholesterol levels in those fed *trans* fatty acids is still unknown. The amount of cholesterol in the erythrocytes was not subject to the influence of dietary fat as has been shown by Monsen *et al.* (22) and Walker and Kummerow (23). This was also true for the present study which indicated that swine fed different dietary fats had the same amount of cholesterol in the erythrocytes. However, the fatty acid composition of the erythrocytes was influenced by the dietary fat content.

It is generally assumed that all of the unesterified cholesterol of plasma can exchange with that of the erythrocytes. Bell and Schwartz (4) found that in swine the maximum exchange erythrocytes and lipoproteins, *in vitro*, occurred between 6–8 hr. Sardet *et al.* (5) have shown that the plasma cholesterol content influenced the interchange rate of plasma and erythrocytes in the guinea pig. It is possible that the higher plasma cholesterol level in those fed hydrogenated fat which contained *trans* fatty acids may cause a slower release rate of cholesterol from the erythrocytes. Differences in geometric configuration, in the chain length, and the degree of saturation of the fatty acid constituents in the erythrocytes may play a role in the functional mechanism of erythrocyte membrane. The *trans* fatty acids that are produced during hydrogenation are deposited in the tissue (24). Decker and Mertz (25) have reported the

incorporation of dietary elaidic acid into lipids of rat erythrocyte stroma. The present study indicated that the *trans* fatty acid content in the erythrocyte obtained from swine fed hydrogenated fat was only 2% of the total lipids. However, the straighter spatial configuration of the *trans*-isomer in the erythrocyte membrane, although the amount was small may alter the permeability characteristics of the membrane.

The release rate of cholesterol from erythrocyte may depend on (1) the amount of cholesterol in the plasma, (2) the fatty acid composition of the erythrocyte, and (3) the presence of *trans* fatty acid in the erythrocyte membrane. These three factors may play a role in the slower release rate of cholesterol from the erythrocyte in swine fed hydrogenated fat which contained *trans* fatty acids.

Summary. Three groups of swine were fed for 8 mo the basal ration; the basal ration plus 17% corn oil or the basal ration plus 17% hydrogenated fat which contained 50% *trans* fatty acids (margarine base stock). The cholesterol content in the plasma was higher in those fed hydrogenated fat diet as compared to those fed the basal or corn oil. However, the cholesterol content in the erythrocytes appeared to be constant regardless of dietary fat. Different dietary fats resulted in considerable differences in the total fatty acid patterns of the plasma and erythrocyte lipids. The release rate of cholesterol from the erythrocytes obtained from swine fed the different dietary fats was compared from cholesterol specific activity changes vs time. The results indicate that the time required to reach 50% equilibration for the erythrocytes and plasma from those fed corn oil, basal diet, and hydrogenated fat was; 1.24, 1.32, and 1.98 hr; respectively. A possible explanation for the slower release rate of cholesterol in those fed hydrogenated fat was given.

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Nutritional Value of Egg Beaters® Compared With "Farm Fresh Eggs"

The Council of Foods and Nutrition,¹ in a statement entitled "Diet and Coronary Heart Disease," has recommended that "In 'risk categories' it is important to decrease substantially the intake of saturated fat and to lower cholesterol consumption." The food industry has attempted to provide high-quality protein food items and for this purpose a new product, "Egg Beaters," has been introduced as a cholesterol-free egg substitute. It contains according to the label statement on the carton "egg white, corn oil, nonfat dry milk, emulsifiers (vegetable lecithin, mono and diglycerides and propylene glycol monostearate), cellulose and xanthan gums, trisodium and triethyl citrate, artificial flavor, aluminum sulfate, iron phosphate, artificial color, thiamin, riboflavin and vitamin D." A comparison of the nutrients in 100 gm of Egg Beaters with the nutrients in 100 gm of "farm fresh eggs" (Table 1) indicates a list of nutrients which should be able to meet the growth requirements of weanling rats.²

METHODS

In order to test this hypothesis, three groups of six lactating female rats each (Sprague Dawley strain), approximately 200 gm in weight, and their 2- to 3-day-old pups (5.4 to 6.8 gm in weight) were transferred from commercial laboratory chow (Purina) to either Egg Beaters, shell eggs, or kept on commercial chow as controls. The females and their young were kept in individual wire cages which contained shredded paper towels for nesting material. The litters were reduced at birth to six pups each; the females were allowed access to water *ad libitum*. For the sake of convenience, 100 shell eggs at a time were cracked into a Hobart mixer, 125 gm of calcium acetate added, blended

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TABLE I
COMPARISON OF NUTRIENTS IN EGG BEATERS® OR
SHELL EGGS WITH NUTRIENT REQUIREMENTS OF
GROWING RATS

Nutrients	100 gm of Egg Beaters	100 gm of Egg	Requirement of Growing Rat, % Diet ²
Protein	11 gm	12.8 gm	13.3 gm
Fat	12.5 gm	11.4 gm	5.5 gm
Calories	166.66	160	GE/day 76 for each rat (444 Kcal/100 gm)
Ca (mg)	81.6 mg	54 mg	560 mg
P (mg)	71 mg	204 mg	440 mg
Na (mg)	181 mg	122 mg	60 mg
K (mg)	213 mg	128 mg	200 mg
Iron (mg)	1.8 mg	2.2 mg	38.9 mg
Cholesterol (mg)	<1.6 mg	550 mg	—
Vitamin A (unit)	1,350	1,180	.67 mg (retinol/Kg)
Vitamin D (unit)	43	50	111.1 (I.U./Kg)
Thiamine (mg)	.13	.1 mg	.14 mg
Riboflavin (mg)	.43	.3 mg	.28 mg
Choline Chloride	*	582 mg	83.3 mg/100 gm
Ca Pantothenate	*	2.7 mg	.89 mg/100 gm
Vitamin B ₆	*	.3 mg	.78 mg/100 gm
Vitamin B ₁₂	*	.001 mg	.00056 mg/100 gm
Biotin	*	.04 mg	.1 mg/100 gm

* Not listed.

for two minutes and stored at -20 C until ready to thaw and feed. Six cartons of Egg Beaters were thawed, 25 gm of calcium acetate added and blended for two minutes in a Hobart mixer. Both mixtures were stored in a refrigerator, poured into 4-oz glass jars and fed daily *ad libitum*. The calcium acetate was added in order to more adequately meet the recommended nutritional requirement for calcium.

RESULTS

The pups from the mothers fed Egg Beaters averaged 31.6 gm, and those fed whole egg averaged 66.5 gm in weight at 3 weeks of age as compared to 70 gm for pups from those fed laboratory chow. Both the mothers and pups fed Egg Beaters



FIG. 1. Weanling rats fed shell eggs (left) or Egg Beaters (right).

developed diarrhea within one week; those fed whole egg did not develop diarrhea. The pups fed the two egg mixtures were weaned at 5 weeks of age. All of those fed Egg Beaters died within three to four weeks after weaning. The general appearance of the rats fed Egg Beaters indicated a gross deficiency in one or more nutritional factors as compared to those fed whole egg (Fig. 1). As the animals had a tendency to become coated with the Egg Beaters, the animals were washed gently with a mild detergent solution and dried with paper towels. The washing removed some of the hair as well as the Egg Beaters (Fig. 2).

COMMENT

Neither Egg Beaters or shell eggs serve as a



FIG. 2. Weanling rats fed shell eggs (left) or Egg Beaters (right). (Both animals were washed with mild detergent, rinsed and dried with paper towels before picture was taken.)

single food source in the human diet. Furthermore, both Egg Beaters and shell eggs are subjected to heat treatment and not consumed in the raw state. In this study, the Egg Beaters and shell eggs were fed in the raw state to indicate whether Egg Beaters has the "nutrition of farm fresh eggs" and to preclude the use of Egg Beaters as a substitute for egg yolk in infant feeding by pediatricians who may consider supplementation with cholesterol-free substitutes early in life in order to prevent the development of atherosclerosis. The rat pups were weaned at 5 instead of the usual 3 weeks in order to provide the advantage of rat milk supplementation for them. However, it is evident that shell eggs, which contain the lipotropic-laden egg yolk, furnish one or more nutritional factors which are absent in Egg Beaters. These nutritional factors are no doubt present in the common food items which comprise the diet of human adults and could probably be added to the Egg Beaters formulation. However, these nutritional factors may not be present in adequate amounts for infants fed milk and Egg Beaters instead of egg yolk from a soft boiled egg. The Council statement¹ under point 3) should be considered: "Care be taken to assure that the dietary advice given does not compromise the intake of essential nutrients." This statement should also be considered in the quest of food items free of cholesterol in the diets of infants.

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Cholesterol and Fatty Acid Synthesis in Swine¹

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ABSTRACT

In incubation studies with swine tissue slices, acetate-1-¹⁴C or glucose-U-¹⁴C as substrates were incorporated more readily into fatty acids and cholesterol in adipose tissue than other tissues tested. Cholesterol and fatty acid synthesizing activity was substantial in the small intestine. When acetate was available, liver, small intestine, and adipose tissue were important sites for cholesterol synthesis. Heart and aortic tissue had marginal levels of cholesterol synthesizing ability. Lipogenesis in adult swine liver, heart, and aortic tissue was extremely low. As in tissue slices, incorporation of acetyl-1-¹⁴C CoA into fatty acids by adipose homogenates indicated high lipogenic activity. Subcellular fractionations of heart and aortic tissue indicated that the heart microsomal fraction had the highest lipogenic activity as measured by the incorporation of acetyl-1-¹⁴C CoA into fatty acids. In adult swine adipose tissue, the incorporation of glucose-U-¹⁴C into fatty acid was higher than its incorporation into glyceride-glycerol. The synthesis of glyceride-glycerol from glucose-U-¹⁴C or acetate-1-¹⁴C in liver was higher than for fatty acid synthesis. The activity of acetyl CoA carboxylase, fatty acid synthetase, citrate cleavage enzyme, nicotinamide adenine dinucleotide phosphate-malate dehydrogenase, glucose-6-phosphate dehydrogenase, and 6-phosphogluconate dehydrogenase was considerably higher in adipose tissue than in other tissues tested, paralleling its high lipogenic capacity.

INTRODUCTION

Using both in vivo and in vitro techniques, it became apparent that the relative contribution of tissue sites to overall cholesterol and fatty acid synthesis varies appreciably depending on

the animal species studied. In the rat and mouse, adipose tissue is the major site of lipogenesis (1-3). However, chick liver contribution to total fatty acid and cholesterol synthesis is far greater than that of adipose tissue (4-7). In swine, it has been found that adipose tissue is the major site for fatty acid synthesis (8,9). Dietschy and Siperstein (10) demonstrated that rat liver has the highest rate of cholesterol synthesis, and gastrointestinal tract ranked second. It has also been found that more than 90% of total cholesterol synthesis occurs in the liver and intestine of the squirrel monkey (11). Romsos et al. (9) indicated that liver and adipose tissue were the most important sites in swine for incorporation of acetate-1-¹⁴C into cholesterol in vivo. Glucose, rather than acetate, is the more important physiological precursor of fatty acid and cholesterol synthesis. However, the relative contribution of tissue sites to cholesterol synthesis with glucose as a substrate in swine is not known, and no estimates of the contribution of other tissue to total cholesterol and fatty acid synthesis in this species has been made. The importance of lipid to arterial tissue in aging and atherosclerosis has long been recognized, and reactions in which the aorta metabolizes lipids are of great interest. It seemed important to investigate the role of different tissues in fatty acid and cholesterol synthesis in swine. Because the mitochondrial fraction represents the major site of fatty acid synthesis in heart and aortic tissue, the synthesis of fatty acids in subcellular fractions in these tissues was also investigated. Furthermore, such information would be important for the study of lipogenic and cholesterologenic adaptations to dietary treatment.

MATERIALS AND METHODS

Animals and Diets

Crossbred weanling swine (Yorkshire x Hampshire) were used in Experiment 1, while Hampshire weanling swine were used in Experiments 2 and 3. Swine in Experiment 1 were fed to 6 months of age the basal diet containing 3% fat and 14.3% protein as furnished by 1,745 lb of ground yellow corn, 200 lb of solvent extracted soybean meal, and 55 lb of a premix of multiple vitamins and minerals per ton of basal ration. (The premix consisted of 5% lysine, 20%

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calcium [calcium carbonate, dicalcium phosphate], 9% phosphorus, 15% sodium and potassium chloride, 0.004% calcium iodate, 0.018% zinc, 0.18% iron, 0.14% manganese as oxides or carbonates, and the following vitamins per lb: 40 mg riboflavin, 100 mg d-pantothenic acid, 300 mg niacin, 2,000 mg choline, 0.32 μ g vitamin B_{12} , a minimum of 60,000 United States Pharmacopeia units of vitamin A palmitate, 60,000 international units (IU) of vitamin D_3 , and 165 IU of vitamin E. In Experiments 2 and 3, the basal diet was supplemented with 200 million units of vitamin D_3 per ton of basal ration for 6 weeks, after which time the vitamin D_3 was withdrawn. The basal diet was then fed for 3 months until the swine were killed. Food and water were available ad libitum.

Tissue Incubation Procedures

For the enzymatic and in vitro incubation studies, liver, adipose, heart, intestine, and aortic tissue samples were obtained immediately after slaughter and placed in 0.9% NaCl during transportation to the laboratory. Adipose tissue samples were obtained from the subcutaneous layer of abdominal fat. The medial and intimal layers of aortic tissue and the mucosal and submucosal layers of small intestine were used for tissue incubation and enzyme assays. Liver, heart, small intestine, and aortic tissue were kept on ice while the adipose tissue was kept at room temperature. Slices of tissues (100-200 mg) were prepared using a Stadie-Riggs hand microtome. The incubation and isolation procedures were similar to the methods described by O'Hea and Leveille (5). Tissue slice incubations were carried out at 37 C in 3 ml of Krebs-Ringer bicarbonate buffer (pH 7.4) under 95% O_2 and 5% CO_2 in a metabolic shaker for 2 hr. Substrates were dissolved in a buffer to a concentration of 10 mM acetate and/or 5 mM glucose. Each flask also contained 0.9 μ Ci acetate-1- ^{14}C or glucose- $U-^{14}C$ and 0.3 unit insulin.

Enzyme Studies

The tissue samples remaining after the preparation of slices were homogenized in four volumes of ice-cold homogenization buffer (pH 7.4) which contained 0.3 M sucrose, 30 mM tris(hydroxymethyl)aminomethane (Tris)-HCl, 1 mM ethylenediaminetetraacetic acid (EDTA), and 1 mM glutathione. The homogenate was centrifuged 60 min at 105,000 \times g, and the supernate fraction (cytosol) was collected and used for the enzyme assay. Enzyme activity measurements were conducted at 37 C in the linear range of activity.

6-Phosphogluconate dehydrogenase (EC 1.1.1.44) was assayed as described by Glock and McLean (12) using the following components: 58 mM glycylglycine buffer (pH 7.4), 10 mM $MgCl_2$, 0.30 mM nicotinamide adenine dinucleotide phosphate, oxidized form ($NADP^+$), and 1.4 mM 6-phosphogluconate.

Glucose-6-phosphate dehydrogenase (EC 1.1.1.49) was assayed by the double substrate method of Glock and McLean (12). The reaction mixture contained 67 mM glycylglycine buffer (pH 7.4), 10 mM $MgCl_2$, 0.3 mM $NADP^+$, 1.4 mM 6-phosphogluconate, and 1.4 mM glucose-6-phosphate.

Nicotinamide adenine dinucleotide phosphate ($NADP$)-malate dehydrogenase (EC 1.1.1.40) was assayed according to the method of Ballard and Hanson (13). Component concentrations were 34 mM Tris buffer (pH 7.3), 1.5 mM $MnCl_2$, 0.3 mM $NADP^+$, and 0.75 mM sodium malate.

Citrate cleavage enzyme (EC 4.1.3.8) was assayed by coupling with nicotinamide adenine dinucleotide (NAD)-malate dehydrogenase according to the method of Takeda et al. (14). The concentrations of reactions components were 200 mM Tris buffer (pH 8.4), 10 mM $MgCl_2$, 10 mM mercaptoethanol, 20 mM citrate, 2 units malate dehydrogenase, 0.2 mM reduced nicotinamide adenine dinucleotide ($NADH$), 10 mM adenosine triphosphate (ATP), 0.2 mM CoA, and 0.3 mM dithiothreitol.

Glycerol-3-phosphate dehydrogenase (EC 1.1.1.8) was assayed according to the method of Gudjarnason et al. (15) using 50 mM triethanolamine-5 mM EDTA, (pH 7.5), 0.2 mM $NADH$, and 1.0 mM dihydroxyacetone phosphate.

Acetyl CoA carboxylase (EC 6.4.1.2) was assayed by the method of Ingle et al. (16). The cytosol fraction (0.24 ml) was preincubated 30 min at 37 C in 0.01 ml of bovine serum albumin (240 mg/ml), and 0.25 ml of a stock solution (40 mM Tris buffer [pH 7.4], 0.4 mM EDTA, 0.4 mM glutathione, 40 mM $MgCl_2$, and 40 mM sodium citrate) in stoppered centrifuge tubes. After preincubation, 0.5 ml of an incubation medium comprised of stock solution, sodium ATP, potassium bicarbonate, and acetyl CoA was added to the reaction vials. The final reaction volume was 1.0 ml (pH 7.4), and component concentrations were 20 mM Tris buffer, 0.2 mM EDTA, 0.2 mM glutathione, 20 mM $MgCl_2$, 20 mM sodium citrate, 2.0 mM sodium ATP, 0.2 mM acetyl CoA, 20 mM potassium bicarbonate (3 μ Ci/ml), and bovine serum albumin (2.4 mg/ml). The reaction was stopped with 0.2 ml of 6 N hydrochloric acid after a reaction time of 10 min at 37 C. After centri-

TABLE I
Relative Rates of Utilization of Acetate-1-¹⁴C by Swine Tissue Slices In Vitro^a

Metabolite measured	Tissue			
	Liver ^b	Adipose ^b	Heart ^c	Aortic ^b
¹⁴ CO ₂	300 ± 15	185 ± 17	176 ± 34	87 ± 25
Fatty acids	1.75 ± 0.30	176 ± 6	0.10 ± 0.01	<0.05
Cholesterol	1.45 ± 0.20	3.0 ± 1.0	<0.1	<0.05

^aResults are expressed as nmoles of substrate converted to the product indicated per 100 mg tissue per 2 hr.

^bMean ± SEM for five swine (average wt 110 kg).

^cMean ± SEM for three swine (average wt 117 kg).

fugation, an aliquot (0.6 ml) of supernatant solution was transferred to scintillation vials and counted in a liquid scintillation counter with 15 ml of counting fluid (7 parts toluene containing 0.4% w/v omnifluor: 6 parts Triton X-100).

Fatty acid synthetase was assayed according to the method of Chang et al. (17). The incubation medium (1 ml) contained 100 mM potassium phosphate buffer (pH 6.8), 0.05 mM acetyl CoA, 0.1 mM malonyl CoA, 1.16 mM reduced nicotinamide adenine dinucleotide phosphate (NADPH), 3 mM EDTA, 2 mM dithiothreitol, and 0.03 μ Ci malonyl-CoA-1,3-¹⁴C₂. The reaction was allowed to proceed 5 min at 37°C for liver and 10 min for other tissues and was stopped with 0.5 ml of 70% HClO₄. Ethanol (1 ml) was added, and the fatty acids were extracted three times with 5 ml portions of petroleum ether (bp 60-68°C) which were transferred to scintillation vials. The combined extracts were dried, and 10 ml of toluene scintillation fluid were added, the samples were counted in a Packard liquid scintillation spectrometer.

In Experiment 3, homogenized samples of heart, adipose, and aortic tissues and subcellular fractions of heart and aortic tissue were used for incubation studies. Samples from adipose and aortic tissues were minced and homogenized in the same homogenization buffer in an omnimixer while samples from heart were homogenized in a Thomas glass homogenizer kept in ice. The homogenates were centrifuged at 1000 \times g for 15 min in a refrigerated International Equipment Co. PR-J centrifuge, and the debris was discarded. The top layer was used for incubation studies. Subcellular fractionation of heart and aortic tissue was accomplished as follows: The 1,000 \times g supernate was centrifuged 30 min at 12,000 \times g to yield a pellet containing the mitochondria. The supernate, after removal of the mitochondria, was centrifuged 60 min at 100,000 \times g to yield the microsomal pellet. The supernate from this spin

yielded the high speed supernate (HSS). The incubation mixture used was a modification of the method of Howard (18). All tubes contained 131 mM glycylglycine (pH 7.4), 6.6 mM glutathione, 0.2 mM NADPH, 1.2 mM NADP, 6.6 mM glucose-6-phosphate, 0.33 units/ml glucose-6-phosphate dehydrogenase, 1.6 mM NADH, 12.9 mM potassium isocitrate, 2.5 mM niacinamide, 5.2 mM MgCl₂, 6.5 mM sodium ATP, 0.65 mM MnCl₂, 6.5 mM creatine phosphate, 0.6 units/ml creatine phosphokinase, 20 mM glycerol-3-phosphate, and 33 mM sodium bicarbonate. Bovine serum albumin (4 mg/ml) was added to the HSS and nonsubcellular fraction tubes. Coenzyme A (0.3 mM) was included in the HSS tube containing acetate-1-¹⁴C and also in all tubes of microsomes and mitochondria containing acetate-1-¹⁴C or acetyl-1-¹⁴C CoA. When acetate was used as the substrate, 6.3 mM acetate-1-¹⁴C (1 μ Ci) was added to the HSS, microsomes, and mitochondria. However, when acetyl CoA was used as the substrate, 0.1 mM acetyl-1-¹⁴C CoA (0.5 μ Ci) was added to the HSS, microsomes, mitochondria, and nonsubcellular fractions. The final volume was 1.0 ml, and incubation was carried out at 37°C with constant shaking for 10, 20, and 60 min in adipose, heart, and aortic tissue, respectively. Protein was determined according to the method of Schacterle and Dollack (19) by the modification of Lowry et al. (20).

RESULTS

Experiment 1

Adipose tissue, with a synthetic rate of 176 ± 6 nmoles per 100 mg tissue per 2 hr, had the highest lipogenic activity of the four different assayed tissues (Table I). Swine liver had a limited capacity for converting acetate to fatty acids, which agrees with the results originally obtained by O'Hea and Leveille (8). The results also show that the ability of adipose tissue slices to convert acetate-1-¹⁴C to fatty

TABLE II

Relative Rates of Utilization of Glucose-U- ^{14}C by Swine Tissue Slices In Vitro^a

Metabolite measured	Tissue ^b		
	Liver	Adipose	Aortic
$^{14}\text{CO}_2$	2.2 ± 0.1	112 ± 16	8.8 ± 3.7
Fatty acids	<0.1	138 ± 14	<0.05
Cholesterol	<0.05	3.0 ± 0.8	<0.05

^aResults expressed as nmoles of substrate converted to the product indicated per 100 mg tissue per 2 hr.^bMean \pm SEM for five swine (average wt 110 kg).

TABLE III

Activity of Pentose Pathway Dehydrogenases and NADP^a-Malate Dehydrogenase in Certain Swine Tissues^b

Enzyme assayed	Tissue			
	Liver ^c	Adipose ^c	Heart ^d	Aortic ^c
Glucose-6-P dehydrogenase	9.4 ± 1.7	161 ± 27	12 ± 2	23 ± 3
6-P-gluconate dehydrogenase	32 ± 3	89 ± 14	12 ± 3	13 ± 4
NADP-malate dehydrogenase	9.9 ± 2	186 ± 12	11 ± 1	9.7 ± 0.3

^aNADH = Reduced nicotinamide adenine dinucleotide.^bActivity expressed as nmoles of substrate utilized per min per mg protein at 37 C.^cMean \pm SEM for five swine (average wt 110 kg).^dMean \pm SEM for three swine (average wt 117 kg).

acid is about 100 times that of liver slices when expressed on an equal wt basis. As also shown in Table I, heart and aortic tissue had a fatty acid synthetic rate considerably lower than that of adipose tissue. The incorporation of acetate- ^{1-14}C into cholesterol was 3.0 and 1.45 nmoles per 100 mg tissue per 2 hr in adipose tissue and liver, respectively. Heart and aortic tissue had marginal levels of cholesterol biosynthesis. Acetate oxidation to CO_2 was much greater in heart and aortic tissue than to fatty acid and cholesterol synthesis. However, the incorporation of glucose-U- ^{14}C into CO_2 was much lower than that of acetate- ^{1-14}C in liver and aortic tissue (Table II). The data revealed that the amount of glucose-U- ^{14}C oxidized to $^{14}\text{CO}_2$ was lowest in liver slices; incorporation of glucose-U- ^{14}C to $^{14}\text{CO}_2$ was only 2% in adipose tissue. Incorporation of glucose-U- ^{14}C into fatty acids (Table II) selected the same pattern but was much lower than that of acetate- ^{1-14}C incorporation into fatty acids. These results indicated that both the rate of CO_2 production and fatty acid synthesis were considerably greater in adipose tissue than in liver and aortic tissue when glucose was used as the substrate.

The results also show that adipose tissue,

with a synthetic rate of 3.0 nmoles per 100 mg tissue per 2 hr, was the most active tissue for cholesterol synthesis when either glucose-U- ^{14}C or acetate- ^{1-14}C was used as the substrate.

The activities of pentose pathway dehydrogenases and NADP-malate dehydrogenase were determined in liver, adipose, heart, and aortic tissues; the data are presented in Table III. Of these four tissues, adipose tissue had the highest dehydrogenase enzymatic activity. Both the pentose pathway dehydrogenases and NADP-malate dehydrogenase were active in adipose tissues. This implies that both pathways are important sources of NADPH in swine adipose tissue. In contrast to adipose tissue, the activity of three dehydrogenase enzymes in liver, heart, and aortic homogenates was extremely low.

Experiment 2

Results of this second experiment confirm previous findings and indicate that swine liver, heart, and aortic tissue have a limited capacity to convert glucose to CO_2 , fatty acids, and cholesterol.

The production of CO_2 from glucose was higher in the small intestine and adipose tissue slices (Fig. 1) than in the other tissues. These data also show that the amount of glucose-

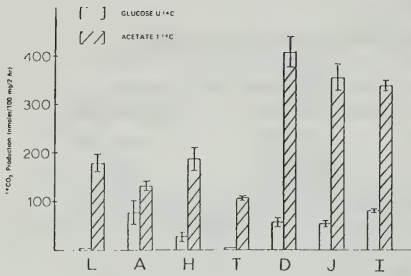


FIG. 1. Incorporation of glucose-U- ^{14}C and acetate-1- ^{14}C into $^{14}\text{CO}_2$ by certain swine tissue slices: L = liver, A = adipose, H = heart, T = aortic, D = duodenum, J = jejunum, I = ileum.

TABLE IV

Incorporation of Glucose-U- ^{14}C and Acetate-1- ^{14}C into Fatty Acids by Certain Swine Tissue Slices^a

Tissue	Substrate ^b	
	Glucose-U- ^{14}C	Acetate-1- ^{14}C
Liver	<0.05	0.73 ± 0.04
Adipose	69 ± 7	82 ± 5
Heart	<0.1	0.11 ± 0.05
Aorta	<0.05	<0.1
Duodenum	2.09 ± 0.39	17.2 ± 5.3
Jejunum	1.77 ± 0.12	25.3 ± 2.4
Ileum	1.34 ± 0.14	16.0 ± 0.7

^aResults are expressed as nmoles of substrate converted to the product indicated per 100 mg tissue per 2 hr.

^bMean ± SEM for three swine (average wt 99 kg).

TABLE V

Incorporation of Glucose-U- ^{14}C and Acetate-1- ^{14}C into Cholesterol by Certain Tissues of Swine^a

Tissue	Substrate	
	Glucose-U- ^{14}C ^b	Acetate-1- ^{14}C ^b
Liver	<0.05	2.10 ± 0.49
Adipose	3.79 ± 0.91	5.80 ± 2.70
Heart	<0.05	<0.05
Aorta	<0.05	<0.05
Duodenum	0.49 ± 0.11	2.25 ± 0.50
Jejunum	0.70 ± 0.10	3.05 ± 0.11
Ileum	0.90 ± 0.36	3.36 ± 1.28

^aResults are expressed as nmoles of substrate converted to the product indicated per 100 mg tissue per 2 hr.

^bMean ± SEM for three swine (average wt 99 kg).

U- ^{14}C oxidized to $^{14}\text{CO}_2$ by all tissues except adipose tissue slices was only a fraction of that of acetate-1- ^{14}C . The oxidation of acetate-1- ^{14}C to $^{14}\text{CO}_2$ was highest in the small intestine

slices (duodenum, jejunum, and ileum).

The relative values for incorporation of glucose-U- ^{14}C and acetate-1- ^{14}C into fatty acids by various swine tissue slices are summarized in Table IV. As in Experiment 1, the incorporation of acetate-1- ^{14}C into fatty acids was much greater than that of glucose-U- ^{14}C . Adipose tissue synthesized the highest amount of fatty acid of all tissues tested. Fatty acid synthetic activity was substantial in small intestinal slices, especially in the case of acetate-1- ^{14}C . Lipogenesis in liver, heart, and aortic tissue was marginal, especially with glucose as the substrate. A comparison of acetate with glucose as a substrate for cholesterol synthesis is presented in Table V. It was found that the incorporation of glucose-U- ^{14}C into cholesterol was much higher in adipose tissue than in any other tissues. Samples from small intestinal slices had substantially higher rates of cholesterol synthesis, especially in the case of acetate. Of the three segments tested, the ileum had the highest rate of cholesterol synthesis. Acetate-1- ^{14}C was readily incorporated into liver cholesterol, whereas the incorporation of glucose-U- ^{14}C into liver cholesterol was not detected. These data also revealed that the incorporation of acetate-1- ^{14}C into heart cholesterol was very low and there was no cholesterol synthesis in heart muscle when glucose was used as the substrate; neither glucose-U- ^{14}C or acetate-1- ^{14}C were incorporated into cholesterol in aortic tissue.

Data on the incorporation of glucose-U- ^{14}C and acetate-1- ^{14}C into glyceride-glycerol by various swine tissue slices are presented in Figure 2. Slices from all tissues were found to actively synthesize glyceride-glycerol. In adipose tissue, glucose was the substrate of choice for glyceride-glycerol synthesis. However, the incorporation of acetate-1- ^{14}C into glyceride-glycerol was higher than that of glucose-U- ^{14}C in liver, heart, and the small intestine; glyceride-glycerol synthesis was about the same in heart and small intestine slices. The incorporation of glucose-U- ^{14}C or acetate-1- ^{14}C into glyceride-glycerol was the lowest in aortic tissue. However, as compared to fatty acid and cholesterol synthesis in aortic tissue, glyceride-glycerol synthesis was extremely high.

The activity of acetyl CoA carboxylase, fatty acid synthetase, citrate cleavage enzyme, and glycerol-3-phosphate dehydrogenase in various swine tissues differed substantially (Table VI). The activity of acetyl CoA carboxylase, fatty acid synthetase, and citrate cleavage enzyme were considerably higher in adipose tissue. These three key enzymes for lipogenesis, as well as pentose pathway dehy-

drogenases and NADP-malate dehydrogenase, paralleled fatty acid synthesis. Citrate cleavage enzyme, presumably involved in the production of acetyl CoA in the cytoplasm, showed the lowest activity in swine liver homogenates. The activities of citrate cleavage enzyme and NADP-malate dehydrogenase (Table III) were low in swine liver, whereas the activity of glycerol-3-phosphate dehydrogenase was extremely high.

Experiment 3

The rate of incorporation of acetyl-1-¹⁴C CoA into fatty acids by homogenates of adipose, heart, and aortic tissues is shown in Table VII. Adipose tissue homogenates, like the tissue

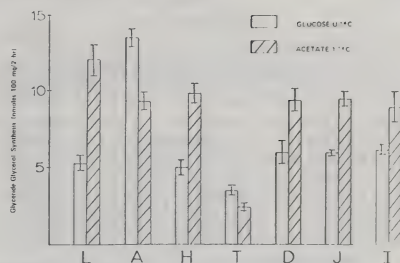


FIG. 2. Incorporation of glucose-U-¹⁴C and acetate-1-¹⁴C into glyceride-glycerol by certain swine tissue slices: L = liver, A = adipose, H = heart, T = aortic, D = duodenum, J = jejunum, I = ileum.

TABLE VI

Activity of Acetyl CoA Carboxylase, Fatty Acid Synthetase, Citrate Cleavage Enzyme, and Glycerol-3-Phosphate Dehydrogenase in Certain Swine Tissues^a

	Liver	Adipose	Heart	Aorta	Duodenum	Jejunum	Ileum
Acetyl CoA carboxylase	0.68	2.56	0.11	0.020	0.20	0.22	0.17
Fatty acid synthetase	0.76	2.32	0.19	0.044	0.15	0.15	0.17
Citrate cleavage enzyme	0.99	19	1.6	2.4	3.9	.. ^b	3.7
Glycerol-3-P dehydrogenase	389	119	224	1.1	9.5	3.6	27

^aActivity expressed as nmoles of substrate utilized per min per mg protein at 37 C. Values represent average of triplicate determinations on pooled tissue cytosol from three animals. See text for details of assay conditions.

^bNot tested.

slices, possessed the highest lipogenic activity of the three tissues tested. Heart homogenates, with a synthetic rate of 4.56 nmoles per mg protein per hr, had a higher rate of incorporation of acetyl-1-¹⁴C CoA into fatty acids than aortic homogenates. When measuring lipogenic activity on an equal wt basis, heart homogenates showed a tremendously high incorporation of acetyl-1-¹⁴C CoA into fatty acids as compared to lipogenesis in heart tissue slices using acetate-1-¹⁴C as the substrate.

Acetyl CoA incorporation into fatty acids was considerably higher in heart microsomes than in aortic tissues (Table VIII). Fatty acid synthesis in the aortic microsomal fraction was slightly higher than that in the high speed supernatant (HSS) and mitochondrial fractions. The synthesis of fatty acids from acetate or acetyl CoA by the HSS or mitochondria in heart and aortic tissue was very low.

DISCUSSION

O'Hea and Leveille (8) have suggested that in vivo more than 99% of de novo synthesis of fatty acids occurs in the adipose tissue of swine when glucose-U-¹⁴C is used as the substrate. However, they studied only the liver and adi-

TABLE VII

Incorporation of Acetyl-1-¹⁴C CoA into Fatty Acids by Homogenates of Adipose, Heart, and Aortic Tissues^a

Tissue	Fatty acid synthesis	
	nmol/mg protein/hr	nmol/100 mg/2 hr
Adipose	76	85
Heart	4.6	23
Aorta	0.009	0.016

^aValues represented average of triplicate determinations on pooled tissues from three animals. See text for details of incubation conditions.

pose tissue. The results presented here agree with the findings of O'Hea and Leveille (8) that adipose tissue is the major site of fatty acid synthesis with both glucose-U-¹⁴C and acetate-1-¹⁴C as substrates in swine tissue slices. When acetate-1-¹⁴C was used as a substrate, the small intestine accounted for a great percentage of overall lipogenesis. This is in contrast to in vivo results obtained with young swine intestines where the fatty acid synthesis represented only a small fraction (1-6%) of the estimated total lipogenesis (9). In vivo studies indicate that young swine liver accounted for 25-30% of the

TABLE VIII

Incorporation of Different Substrates into Fatty Acids by Subcellular Fractions of Swine Heart and Aorta^a

Tissue	Substrate	Concentration (mM)	HSS ^b	Microsomes	Mito-chondria
Heart	Acetate-1- ¹⁴ C	6.3	9	37	20
	Acetyl-1- ¹⁴ C CoA	0.10	10	11,940	10
Aorta	Acetate-1- ¹⁴ C	6.3	12	33	33
	Acetyl-1- ¹⁴ C CoA	0.10	8	18	1

^aActivity expressed as μ moles of substrate utilized per mg of protein per hr at 37 C. Values represent average of triplicate determinations on pooled tissue from three animals. See text for details of incubation conditions.

^bHSS = High speed supernatant.

newly synthesized fatty acids (synthesis occurring in liver and adipose tissue only) when acetate-1-¹⁴C was injected into the vena cava (8). However, in these studies, the synthesis of fatty acids in adult swine liver was very low, even when acetate was used as the substrate. The synthesis of fatty acids in heart and aortic tissue was also very low with both glucose-U-¹⁴C and acetate-1-¹⁴C as substrates. Subcellular fractionations of heart and aortic tissue possessed high fatty acid synthetic activity in the microsomal fraction. Because the microsomal elongation system is well developed in the rat and rabbit, it seems possible that, in swine heart and aortic tissue, the elongation system is more important than de novo synthesis of fatty acids.

The NADPH produced mainly in the pentose pathway dehydrogenases and NADP-malate dehydrogenase is used to reduce acetyl CoA for fatty acid biosynthesis (21). The activity of these enzymes in swine adipose tissue is high, paralleling its high lipogenic capacity. This implies that they may serve an important function in the production of reducing equivalents for fatty acid synthesis in this tissue. In contrast, the low activity of the three dehydrogenase enzymes in liver, heart, and aortic tissue may be due to their limited capacity to generate NADPH.

The activity of acetyl CoA carboxylase and fatty acid synthetase were highest in swine adipose tissue of ca. equal activity in all of the tissues observed in this study. The activities of citrate cleavage enzyme, NADP-malate dehydrogenase, and pentose pathway dehydrogenase were higher in adipose tissue than any other tissues tested, which is in agreement with the concept that adipose tissue is the primary site of fatty acid biosynthesis. Activity assayed as fatty acid synthetase and acetyl CoA carboxylase was found in all tissues. The activity could represent chain elongation activity

normally found in mitochondrial and microsomal fractions inasmuch as tissue homogenization conditions were extreme, especially in the case of tough aortic tissue.

In adult swine, adipose tissue appears to be an important site for cholesterol synthesis; the small intestine ranked second, while liver, heart, and aortic tissue possessed marginal levels of cholesterol synthesis when glucose was used as a substrate. When acetate is available, liver, small intestine, and adipose tissue are important sites for cholesterol synthesis. This is in contrast to the results obtained with young swine in vitro where the intestine contributed only about 4% of the total cholesterol synthesized from acetate-1-¹⁴C, whereas liver and adipose tissue contributed 67 and 29%, respectively (9). In the small intestine, the ileum seems to be higher in cholesterol synthesizing ability than the duodenum and jejunum. This is in agreement with the results obtained with rat, monkey, and human intestine where sterol synthesis was greater in the ileum than in the jejunum (10,11,22). However, this is in contrast to in vivo results obtained from young swine; the upper three segments of the small intestine contributed more to intestinal cholesterol synthesis than the lower segment (9).

Although glucose cannot be converted to cholesterol in swine liver slices, a substantial amount of acetate-1-¹⁴C was incorporated into liver cholesterol. Apparently, free acetate is required for cholesterol synthesis in swine liver. It has been reported that organic acids such as acetic, propionic, and lactic acid are produced by microorganisms in the digestive tract of swine (23,24), appear in the blood stream (25,26), and are removed by the liver (26). Swine liver possesses an active acetyl CoA synthetase enzyme (27) which could activate acetate of endogenous or exogenous origin and make it available for the synthesis of cholesterol.

Glucose is also an important source of glycerol-3-phosphate for lipid synthesis in adipose tissue (28). The present results indicate that there was a higher incorporation of glucose-U-¹⁴C and acetate-1-¹⁴C into fatty acids than glyceride-glycerol in adult swine adipose tissue. This agrees with the findings of Mersmann et al (29) that glucose was incorporated equally into fatty acids and glyceride-glycerol before weaning, with a shift toward fatty acids as the primary product after weaning, whereas acetate was mainly incorporated into fatty acids at all ages in swine adipose tissue.

The greatest production of CO₂ from acetate by small intestine preparations in swine probably reflected the highest mitochondrial activity. Although fatty acid synthesis is low in aortic tissue, it might have high mitochondrial activity as reflected by the high CO₂ production from acetate.

When glucose-U-¹⁴C is used as the substrate for fatty acid and cholesterol biosynthesis in swine, citrate cleavage enzyme is necessary for the conversion of citrate to acetyl CoA. The very low activity of citrate cleavage enzyme in swine liver presumably led to the marginal levels of cholesterol and fatty acid synthesis using glucose as precursor. Because glucose is the main substrate absorbed by nonruminant animals, the results obtained with glucose-U-¹⁴C may more nearly reflect the actual situation than results obtained when acetate-1-¹⁴C was used as the substrate for fatty acid and cholesterol biosynthesis in swine.

Subcellular fractionation indicated that microsomal fractions in heart and aortic tissue had higher fatty acid synthesizing ability than the high speed supernate and mitochondrial fractions. Similar results were also found in squirrel monkey aorta when acetyl-1-¹⁴C CoA was used as the substrate (18). However, Whereat (30) and Whereat et al. (31) demonstrated that the mitochondria were the most important sites of synthesis in rabbit heart and aorta for the incorporation of acetate-1-¹⁴C into fatty acids. Low fatty acid synthesis in aortic tissue slices and homogenates indicated that swine aortic tissue was not an important site for lipogenesis.

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Current Studies on Relation of Fat to Health¹

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ABSTRACT

An increase in the linoleic to oleic acid ratio by an increase in the percentage of the polyunsaturated $\omega 6$ family of fatty acids in culinary fats and a decrease in the consumption of cholesterol-rich food were believed necessary as a prerequisite to early intervention in coronary heart disease. A decrease in total fat consumption also has been recommended. However, a decrease in the percentage of fat in the diet may not be nutritionally sound, as it may only increase the percentage of carbohydrates consumed and, thus, the synthesis of the $\omega 9$ family of fatty acids from the surfeit calories. It may be more judicious to decrease the total number of calories through less consumption of a well balanced diet. Furthermore, as the *trans*-fatty acids, which are formed during hydrogenation, are not discriminated against completely by acyl-glycerol-3-phosphoryl-choline transferase or acyl coenzyme A cholesterol transferase, it would be, from a biological viewpoint, advantageous to eliminate *trans*-fatty acids from both stick and tub type margarines.

INTRODUCTION

It is evident that fats and oils supply an economical source of calories to the American diet. However, it is also evident that the level of fat intake, the mixed fatty acid composition of the fat, and the character of the sterols in the fat or oil may all have a nutritional impact. Laboratories located in every one of the five continents are engaged in determining the extent of this impact upon heart disease and stroke, the leading cause of death in every country that keeps mortality records.

ROLE OF LIPIDS IN DISEASES OF LONGEVITY

To understand the relationship of cancer, heart disease, and stroke to mortality, it is important to recognize that a shift in death rate/100,000 of population has occurred since 1900 (1). The diseases caused by bacteria or viruses have been controlled by antibiotics, so that cancer, heart disease, and stroke are responsible for 81.6% of all deaths in the U.S. A task force of the National Cancer Institute has just completed an intensive study on how best to conquer cancer and has asked for additional funding (2).

Cancer represents a complex disease process. At a recent symposium on "Molecular Biology and Pathology," it was stated that the cancer cell is capable of a higher rate of glycolysis than a normal cell. However, Potter (3) stated, "Pick any enzyme whose activity is modulated in the normal cell of origin, and there is a good chance that it will respond in a peculiar fashion in the neoplasm."

The fat and oil industry has a stake in the future direction of cancer research, as neither the mechanism that converts a normal to a malignant cell nor the mechanism that might be useful in controlling the key enzyme presently is known. It is known that oxidized sterols (4) and complex cyclic sterol-like hydrocarbons, such as methyl cholanthrene and dibenzanthracene, are carcinogenic, i.e. capable of converting a normal to a malignant cell

(5). However, it is not known whether the methyl silicone, propylene glycol monostearate, or the mono- and diglycerides in shortenings aid in the absorption of oxidized sterols. This is an area of research that deserves further effort.

Pearce and Dayton (6) indicated that an experimental group of human subjects, fed diets which contained polyunsaturated fats, developed more tumors than subjects fed saturated fats. This is an interesting observation in light of the results of Nichaman, et al., (7) that dietary linoleate stimulated the conversion of linoleic acid to carbon dioxide and that linoleic acid is more readily metabolized in rats fed corn oil than in those fed coconut oil (8). It would be worth further study to determine whether polyunsaturated fatty acids (PUFA) influence the rate of glycolysis or the assembly of cell membranes in malignant cells.

In a recent review, Reiser (9) has critically discussed the complex interrelation between plant sterols and polyunsaturated and saturated fats and concluded that saturated fats do not increase serum cholesterol levels significantly. As an elevated serum cholesterol level has been considered an important risk factor in the development of coronary heart disease, the conclusions of Reiser warrant serious consideration. However, at least two parameters that were not taken up in this review also may be relevant to the development of atherosclerosis. They are: (A) the tissue level of polyunsaturated fatty acids on a minimum linoleic acid intake and (B) the possible role of *trans*-fatty acid upon the biophysical properties of cell membranes.

NUTRITIONAL AND PHYSIOLOGICAL PROPERTIES OF PUFA

That PUFA occur in families or series in which the terminal structures are similar is now widely recognized. Original studies in this area, as well as further investigations of the metabolic conversions of several families of PUFA, have been reported by Klenk (10-12). These fatty acids include the mono-, di-, and polyenes of the $\omega 6$, $\omega 7$, and $\omega 9$ families and of chain lengths C_{20} - C_{22} . With respect to the $\omega 6$ acids, rats fed diets rich in linoleate (corn oil), or barely adequate with respect to this acid (tallow or butterfat), resulted in almost equal levels of $\omega 6$ long chain unsaturated fatty acids in the cholesterol esters and phospholipids (Table I) in the isolated tissues (13). Therefore, the sum total of the $\omega 6$ family of fatty acids in a given tissue and lipid class does not necessarily bear a direct relationship to the quantitative level of linoleic acid in the diet. However, dietary linoleate is known to lead to increased levels of the members of the $\omega 6$ family, especially

TABLE I

Dietary Fat and Total Fatty Acid Composition Greater than C_{18} in Cholesteryl Esters and Phospholipids in Heart Tissue (13)^a

Dietary fat	Cholesteryl esters		Phospholipids	
	$\omega 9$	$\omega 9$	$\omega 9$	$\omega 9$
Corn oil	6.9	8.7	—	23.6
Milk fat	9.4	38.5	—	32.0
Beef tallow	4.3	4.9	4.9	31.6
Hydrogenated fat	19.8	7.5	3.3	17.8
Fat free	18.1	16.5	22.4	12.8

^aResults are summation of total $\omega 9$ and $\omega 6$ fatty acids, respectively, and are expressed as percentage of total fatty acids.

¹One of five papers presented at the symposium, "Status of Fat in Food and Nutrition," AOCs Fall Meeting, Chicago, September 1973.

TABLE II

Acyl-Coenzyme A Cholesteryl Ester Acyltransferase
Activity in Rat Liver Microsomes (45)

Diet	Enzyme activity ^a
Stock	25.0
Corn oil	29.0
Fat-free	8.0
Hydrogenated fat	10.0

^aExpressed in millimicromoles cholesterol esters synthesized/mg protein/hr.

arachidonic acid (20:4 ω 6), in cholesteryl esters and phospholipids (14,15). The absolute ω 6 concentrations in heart tissue were generally higher in the phospholipids than in the cholesteryl esters and were largely accounted for by high levels of 20:4 ω 6. Tissue fatty acid specificity was also evident; for instance, relatively high amounts of 22:4 ω 6 were seen only in the adrenal cholesteryl esters. This observation has been reported by other workers (16,17). Furthermore, Walker has shown that corn oil supplementation of a fat-free diet resulted in increased levels of the ω 6 acids with time of supplementation in the total lipids of rat liver, heart, and plasma (18,19). There was a simultaneous decrease in the level of the ω 9 series of fatty acids.

TRANS-FATTY ACIDS AND THE BIOPHYSICAL PROPERTIES OF CELL MEMBRANES

An extensive literature has been developed in regard to cell membrane configuration, and various types of models have been suggested to represent the manner in which lipids are incorporated or sandwiched into bilayers with protein (20-24) at the cellular level. All of them agree that the phospholipids and cholesterol in cell membrane seem to line up in tightly bound columns with hydrophobic and hydrophilic orientation and that the fatty acid structure could influence the properties of cell membranes. For example, Chapman, et al., (20) found that the replacement of a *cis*- by a *trans*- acid in the 2 position of phosphatidylethanolamine or phosphatidylcholine caused monomolecular films to be appreciably more condensed in character in vitro. The association of cholesterol with *trans*-phospholipids also was believed to differ from the association of cholesterol with the isomeric *cis*-phospholipids. Mulder and Van Deenen (21) have shown that there is a free interchange, in vitro, of fatty acids between the lipids in the plasma and the lipids in the red blood cell. Demel and Eibl and coworkers (22,23) also have shown that even a difference in chain length and the degree of unsaturation of the incorporated fatty acids influenced the interfacial characteristics of phospholipids significantly. The classical studies of Burr and Burr (24) and Holman (25) provide examples for the importance of the ω 6 series of fatty acids to the rate of water transpiration through skin tissue.

Many studies have been designed to correlate the role of dietary fat with the biophysical properties of the lipids in the arterial mesenchyme. One of the most interesting and potentially significant studies involved the use of elaidinized olive oil by McMillan, et al. (26-28). He reported that rabbits "fed elaidinized olive oil showed a little more visible atherosclerosis of the aortic arch, but no more atherosclerosis in the thoracic and abdominal aorta. They had a somewhat higher total cholesterol content per aorta in their aorta than did those rabbits fed natural olive oil and cholesterol." As ca. 60% PUFA in soybean oil are elaidinized during catalytic hydrogenation, such *trans*-isomers of oleic and linoleic acid are present in the shortenings and margarines that provide the major source of the visible fat in the American diet. The high polyunsaturated fatty acid

TABLE III

Concentration of Elaidate in Lipid Classes of
Heart and Plasma Lipoproteins
(Wt% of Elaidate of Total Fatty Acids of Fraction) (46)

Lipids ^a	15 Weeks	20 Weeks
Heart		
Total lipids	10.6 (10.5-10.7) ^a	16.8 (16.2-17.4)
CE	11.2 (10.9-11.5)	4.2 (4.0-4.4)
TG	10.8 (10.6-11.2)	11.3 (10.9-11.7)
FFA	9.7 (9.4-10.2)	10.5 (10.0-11.0)
PL	15.8 (15.4-16.1)	10.4 (10.3-10.7)
Plasma lipoproteins		
Total lipids	17.9 (17.5-18.3)	17.5 (17.2-17.8)
VLDL:		
CE	7.8 (7.5- 8.1)	16.2 (15.8-16.5)
TG	18.6 (18.2-19.0)	39.5 (38.8-40.0)
FFA	10.2 (9.6-10.8)	21.9 (21.8-22.3)
PL	9.1 (9.0- 9.3)	18.3 (18.1-18.5)
LDL:		
CE	7.1 (7.0- 7.2)	2.1 (2.0- 2.2)
TG	14.0 (13.6-14.4)	17.0 (16.8-17.2)
FFA	14.9 (14.3-15.4)	7.3 (7.1- 7.5)
PL	6.0 (5.9- 6.3)	23.3 (23.0-23.6)
HDL:		
CE	8.8 (8.6- 9.0)	3.9 (3.8- 4.0)
TG	15.3 (14.8-15.6)	10.4 (10.0-10.8)
FFA	2.2 (2.2- 2.2)	23.4 (23.1-23.8)
PL	19.0 (18.5-19.4)	11.7 (11.3-12.0)

^aAbbreviations: VLDL = very low density lipoprotein, LDL = low density lipoprotein, HDL = high density lipoprotein, CE = cholesterol ester, TG = triglyceride, FFA = free fatty acid, and PL = phospholipid. Range of values in parentheses.

margarines still contain ca. 20% *trans*-fatty acids.

Trans-unsaturated fatty acids have been shown to oxidize as readily to CO₂ as do their *cis*-isomers (29,30). However, anabolism or elongation of the *trans*-fatty acids seems to be selective. The *cis*-9,*trans*-12 octadecadienoic acid has been reported (31) to elongate to an isomer of arachidonic acid believed to be *cis*-5,*cis*-8,*cis*-11,*trans*-14 eicosatetraenoic acid, and *trans*,*trans*-linoleic acid seemed to elongate to *cis*-5,*cis*-8,*trans*-11,*trans*-14 eicosatetraenoic acid (32). Selinger and Holman (33) found that *trans*,*trans*-linoleic acid did not increase the level of PUFA normally derived from the *cis*,*cis*-isomer. The studies of DeThomas, et al., (34) indicated that elongated nonessential fatty acids can esterify the β -position in lecithin. However, a number of studies (35-37) have demonstrated that *trans*,*trans*-linoleic acid cannot function as an essential fatty acid, presumably because its elongated derivative does not have the functional characteristics of the elongated *cis*,*cis*-isomer.

Privett and Blank (38) reported that the *cis*,*trans*-isomer depressed the conversion of *cis*,*cis*-linoleic to arachidonic acid (to 33%) as did the *trans*,*cis*-isomer (to 12%), although not so drastically as the *trans*,*trans*-isomer (to 1.4%). The presence of 50% *cis*,*cis*-linoleic acid did not counteract completely the depressing effect of *trans*,*trans*- (13.5%) or *cis*,*trans*- (17.5%) linoleic acid on the conversion of linoleic to arachidonic acid. The major share of the arachidonic acid was present in an α -saturated, β -tetraene triglyceride. In animals that had been fed *cis*,*trans*- or *trans*,*trans*-linoleic acid, the percentage of arachidonic acid incorporated at the β -position was depressed greatly when compared with that of animals fed *cis*,*cis*-linoleic acid (14.1, 1.6, and 42.4%, respectively). In those fed *cis*,*trans*-linoleic acid, an almost equal amount (12.5%) trienoic acid was incorporated at the β -position (39).

In a series of studies in our laboratory (40-42), Sgoutas found that the cholesterol esterases in the microsomal and soluble fractions of rat liver hydrolyzed the ¹⁴C-cholesterol esters of *cis*- and *trans*-octadecenoic and octadecadienoic acids at different rates. The substrate concentration curves of the hydrolysis of cholesteryl-oleate, -linoleate, -elaidate,

-linelaidate, -palmitate, and -stearate by the soluble enzyme fractions showed that unsaturated cholesterol esters were hydrolyzed faster than saturated ones, agreeing with previous reports. Sgoutas also showed that the unsaturated esters clearly were divided into two groups: those with *cis*-double bond and those with *trans*-, with the former being hydrolyzed more rapidly than the latter. The substrate concentration curves indicated that the order of their hydrolysis by the soluble protein fraction was: *cis*-unsaturated > *trans*-unsaturated > saturated cholesterol esters. A similar pattern of substrate preference was observed when the crude soluble fraction or the microsomal fraction was used as the enzyme source. Rat liver microsomes also have been shown (43,44) to contain an enzyme system that esterifies cholesterol in the presence of adenosine 5'-triphosphate (ATP) and coenzyme A (CoA). When this enzyme system was obtained from the liver, microsomes of rats that had been fed a hydrogenated fat of 48% *trans*- and 0% essential fatty acid content, a decrease in the ability of these liver microsomes to esterify ^{14}C -cholesterol in vitro (Table II) was observed (45).

At comparable time periods, rats fed hydrogenated fat contained significantly more heart lipids than those fed beef tallow (46). *Trans*-fatty acid (elaidate) concentration in the lipid classes was variable, especially among the lipoprotein classes, and was not a direct function of the duration of feeding (Table III). Plasma very low density lipoprotein lipid classes indicated a doubling of elaidate concentration of each lipid class from 15-20 weeks of fat feeding. Also, at both time intervals, there was a consistent trend in the levels of elaidate in the four lipid classes, the order being triglyceride > free fatty acid > phospholipid > cholesterol ester. These two observations were not seen so clearly in the lipid classes of low density lipoproteins and high density lipoproteins. These results suggest differences in the mechanism of incorporation and turnover of elaidate, not only in different tissues, but also among the major lipoprotein types. Similar results were noted in the plasma lipoproteins obtained from swine fed hydrogenated fat (47) and in human tissue (48). Human adipose tissue was found to contain from 2.4-12.2%; liver, 4.0-14.4%; heart, 4.6-9.3%; and aortic tissue, 2.3-8.8% of *trans*-fatty acids.

The human diet contains a mixture of dietary fats that presumably supply an adequate amount of linoleic acid; yet, human adrenal cholesterol esters do contain some elongated $\omega 9$ series of fatty acids which may indicate the presence of less than an optimum level of dietary $\omega 6$ fatty acids (Table IV). The percentage of total $\omega 9$ polyunsaturated C_{18} and C_{20} fatty acids in the human adrenal (49,50) was in the same approximate range as found in rats fed 20% hydrogenated fat and 2% corn oil, or 8% and 14%, respectively. The adrenal cholesterol esters from rats fed corn oil contained only 3.0% while those fed only hydrogenated fat contained 34% $\omega 9$ fatty acids. The total $\omega 6$ fatty acids of human adrenal lipids was comparable in amount to that found in rats fed 2% corn oil. Corticosterone is the major corticosteroid of the rat adrenal tissue (51,52), and it has been suggested that essential fatty acid deficiency status leads to a decreased ability of rat adrenals to synthesize corticosteroids (53,54). Recent in vitro studies utilizing the endogenous free cholesterol present in the adrenals have shown that the ability for corticosteroidogenesis was dependent upon the nature of the antecedent dietary fat (55). If adrenal corticosteroid synthesis is modified by the nature of the dietary fat under in vivo conditions, its influence on corticosteroidogenesis could have important implications for some key aspects of carbohydrate, protein, and lipid metabolism (56).

POSSIBLE APPLICATIONS OF LIPID RESEARCH FINDINGS TO HUMAN DIET

It is evident that a dietary source of $\omega 6$ fatty acids is

TABLE IV
Composition of Adrenal Cholesterol Esters

Obtained from rats fed:	Percent total polyunsaturated $\text{C}_{18} + 20$ fatty acids	
	$\omega 6$	$\omega 9$
20% Hydrogenated fat (46)	3.4	34.2
20% Hydrogenated fat + 2% corn oil	9.1	14.2
20% Corn oil	29.5	3.0
Human (49)	24.9	8.3
Human (50)	7.0	4.9

essential to proper cell membrane structure and function and that an excessive intake of polyunsaturates may lower serum cholesterol levels. However, there is no evidence that the excess consumption of linoleic acid contributes to the prevention of heart disease (57). The coating of linoleic acid containing dairy feed stuffs with formaldehyde to produce a higher linoleic acid containing butterfat (58) or the incorporation of drugs into poultry feeds to depress cholesterol biosynthesis in a laying hen with the hope of producing egg yolks of lower cholesterol content (59) represents an interesting research approach. However, on a practical commercial basis, it would be far more economical to produce margarines and shortenings of higher linoleic acid content. A stick type margarine easily could contain at least 25% linoleic acid. Furthermore, as *trans*-fatty acids are not discriminated against completely by acyl-glycerol-3-phosphoryl-choline transferase or acyl CoA cholesterol acyltransferase, it would be, from a biological viewpoint, advantageous to eliminate *trans*-fatty acids from both stick and tub type margarines. *Trans*-fatty acid free margarine base stocks could be fabricated from completely hydrogenated soybean oil and corn or cottonseed oil by a rearrangement process presently in use for the improvement of the shortening value of lard and which already is being used in The Netherlands, Germany, Sweden, and Finland for the production of a *trans*-free high PUFA margarine. The rearrangement process may add to the cost. However, in view of the need for an optimum level of the biologically functional $\omega 6$ series of fatty acids, it would seem judicious to eliminate the *trans*-type of unsaturated fatty acids from all dietary fats. It also would seem judicious to get away from the term all purpose shortening, to provide heat-stable frying fats devoid of mono- and diglycerides, to provide baking fats that do not contain methyl silicone, to provide salad oils that do not contain polymerized winterizing agents, and to provide emulsified food substitutes that contain less than 1% propylene glycol monostearate.

A great concern has been expressed in regard to the air we breathe, the water we drink, and the food additives we eat. It is also possible that the kind of fats we eat may be important to the complex and subtle biological process that cause the deposition of lipids into the arteries of all human beings. It is difficult to make diet recommendations in the face of a problem as complex as atherosclerosis. It is evident, however, that the popular habit of consuming high calorie snack items by someone who is already overweight will only add fat and cholesterol to the serum and tissue. However, dietary fats are essential as a sufficient intake of the $\omega 6$ series of fatty acids is necessary to prevent the elongation and incorporation into phospholipids and cholesterol esters of the *trans*-fatty acids or of the $\omega 9$ series of fatty acids that are synthesized from carbohydrates.

It is also necessary to provide an adequate protein intake, as carrier protein is necessary for the synthesis of lipoprotein. It is unfortunate that the shopper in a modern supermarket can purchase hundreds of food items that will satisfy caloric requirements but not the protein or other

nutrient requirements. It may be possible to satisfy protein requirements by the consumption of unrefined whole grain cereals, legumes, and leafy vegetables. However, in a high calorie diet, such as the American diet, only meat, milk, and eggs can supply a sufficient amount of protein for daily needs. These protein sources admittedly contain either saturated fats or cholesterol. Under normal conditions, the enzyme system that is available for the metabolism of lipids will metabolize the saturated fatty acids and cholesterol that is not needed for tissue maintenance. However, the influence of a dietary source of cholesterol upon human serum cholesterol levels, very low density serum lipoprotein levels, and heart disease needs further clarification. The use of crystalline cholesterol or powdered egg yolk in experimental diets to increase serum cholesterol levels is not analogous to the use of a whole egg which contains egg white protein in addition to egg yolk protein, polyunsaturated fats, and cholesterol.

The best that can be done at present for the majority of human subjects is for them to eat a well-balanced diet of cereals, fruits, vegetables and enough meat, milk, and eggs to provide for an adequate protein intake. Heart disease seems to be due to an exceedingly complex metabolic interrelationship. Yet, the rate of incidence may be decreased by eating a well-balanced diet, by providing biologically utilizable polyunsaturated fats, by taking enough exercise to provide for good muscle tone, by getting enough rest, and by avoiding cigarettes. Epidemiological studies indicate that the human subjects in population groups that follow such a regime have less heart disease than those who do not.

CHARGE TO THE EDIBLE FAT AND OIL INDUSTRY

The fat and oil industry should provide the leadership to more adequate funding of not only its own research laboratories but also of governmental and university laboratories. The present practice of spending large sums of money to provide a few percentage increase in sales over a competitor may be nonproductive, as the advertising costs could cancel out the additional money provided by an increase in sales. Furthermore, the added costs due to advertising are paid ultimately by the consumer. The new Food and Drug Administration labeling requirements may solve this problem for any consumer that will take the time to compare cost with the percentage composition on the label. It would serve both the industry and the public if the industry itself combined resources under the auspices of the AOCS and decided to solve common problems, such as the development of hydrogenators that do not use millions of cubic feet of natural gas every day as a source of hydrogen, the objectionable odors from deodorizers, and better means of disposing of bleaching earth. Methods should be developed to hydrogenate soybean oil by other means; objectionable odors could be removed with oxidizers, and bleaching clays can provide valuable by-products. Such an approach would provide for an acceptable public image and also may persuade the U.S. Congress and the Food and Drug Administration that the industry is genuinely interested in its own welfare.

The fat and oil industry should realize that a fundamental change in research funding has taken place within the grant-in-aid program at the National Institutes of Health. The emphasis is now on mission-oriented heart and cancer research, rather than on fundamental science. However, this emphasis should represent an addition of funds rather than a shifting of funds within the various Institutes of the National Institutes of Health. Millions of people still suffer from arthritis, as an example, and funds that are provided by the National Institute for Arthritis and

Metabolism may provide as many clues to the cause of heart disease or cancer as funds that are provided by the National Heart and Lung Institute or the National Cancer Institute.

Both the National Research Council of the National Academy of Sciences and the Council of Nutrition of the American Medical Association recently have recommended a decrease in total fat consumption (60). Such a recommendation may not be nutritionally sound, as it may only increase the consumption of carbohydrate and, thus, the synthesis of $\omega 9$ fatty acids from the surfeit calories. It would be more economical to stay at our present percentage level of total fat intake and decrease the number of calories through less consumption of a well balanced diet.

Cancer and heart disease are complex diseases that will require a tremendous research effort for their solution. The fat and oil industry should become more actively involved in this effort for its own sake, as well as for the sake of the consumers of fabricated products of this industry. These products should be reexamined by means of the sophisticated techniques which have become available to lipid laboratories, and every avenue of their possible impact upon cancer and heart disease should be explored thoroughly.

We hope to increase our own efforts in this direction through an additional research facility. This facility, a commercial swine farm which has been made available to us on the basis of a 99 year lease by the Harlan E. Moore Heart Research Foundation, currently is housing 240 swine on 10 different diet patterns. Some of these groups are being fed a source of *trans*-fatty acids and should provide tissue for *in vitro* studies of the type currently in progress in De Kruffy's laboratory (61). An additional breeding facility will be available in the future. This breeding facility will allow the use of 800 purebred swine/year. The blood or tissue from these animals will be available on a no cost basis to any research group that is interested in such tissue.

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SYMPOSIUM: Nutritional Perspectives and Atherosclerosis

LIPIDS IN ATHEROSCLEROSIS

THE ROLE that individual foods play in the nutritional perspective, that is, their actual role, in atherosclerosis is still not clear. Recommendations are being made and conclusions drawn without knowledge of all the factors involved. For example, the final report of the National Diet Heart Study (1968) stated "Extensive evidences implicate diet as a key factor in the etiology of atherosclerosis and suggests that the disease can be prevented by changes in diet, particularly by lowering serum cholesterol level." In addition, a recent policy statement of the American Medical Association Council on Food and Nutrition (1972) and the Food and Nutrition Board of the National Academy of Sciences indicated how changes in diet could be accomplished: "Generally such lowering can be achieved most practically by partial replacement of the dietary sources of saturated fat with sources of unsaturated fat, especially those rich in polyunsaturated fatty acids." This joint statement concluded: "There is abundant evidence that the risk of developing CHD [cardiovascular heart disease] is positively correlated with the cholesterol in the plasma." Further research indicates that these statements do not reflect the full picture. Such a nutritional perspective has not fully considered that dietary sources of saturated fat and cholesterol, that is, meat, eggs and dairy products, serve as the major source of protein, vitamins and minerals in the American diet (Connor et al., 1968). It has been assumed that less cholesterol is deposited in the arteries when the serum cholesterol level is lowered by the addition of polyunsaturated fats to the diet, an assumption that cannot be tested in human subjects.

POSSIBLE ROLE OF LIPIDS IN DEVELOPMENT OF ATHEROSCLEROSIS

THE ASSUMPTION that a high serum cholesterol level accelerates the development of atherosclerosis has been found valid in many studies on experimental animals. The high serum cholesterol levels can be obtained by feeding animals high fat diets which contain 1-2% crystalline cholesterol, or a cholesterol intake equiv-

alent in man to the consumption of 30-60 eggs/day. However, this assumption does not explain the development of CHD in subjects with serum cholesterol levels below 250 mg %. Another explanation for the development of CHD in these subjects may possibly be found in the character of the dietary fats we consume as well as other yet unknown factors.

It has been shown that the endothelium layer of the abdominal aorta can be ruptured mechanically by inserting an inflatable balloon into the upper femoral artery and pushing it upward into the aorta. Lipids infiltrate the smooth muscle cells adjacent to the ruptured endothelium layer of cells to produce changes similar to those noted in the development of atherosclerosis (Nam et al., 1973). Furthermore, Dr. H. Imai, of the Albany Medical School, who is working with us on our studies on swine atherosclerosis, has found dead cells within the layer of smooth muscle cells in the intima and media of newly born swine (personal communication).

Immunological evidence indicates that the very low density lipoprotein fraction of the serum furnishes the lipids that accumulate in the intima layer of the aorta. However, studies with radioactively labeled components have shown that both lipid infiltration and lipid synthesis *in situ* can occur in isolated arterial tissue. The incorporation of ^{32}P -phosphate and ^{14}C -choline into normal and atherosclerotic rabbit aortas has been studied *in vitro* (Newman et al., 1966). The same results as observed *in vivo* were found, namely an enhanced synthesis of phospholipids by the atheromatous aorta, localized primarily in the intima. The difference in distribution of ^{32}P between the two most active phospholipid classes, phosphatidylcholine and phosphatidylinositol, of normal and atherosclerotic aortas was similar *in vivo* and *in vitro*. In the normal aorta, phosphatidylinositol had a higher percentage of ^{32}P than phosphatidylcholine; in the atheromatous aorta, these percentages were reversed. The studies *in vitro* were used as evidence to show that the enhanced synthesis observed *in vivo* was probably not mediated by neural factors or stretch of the aorta, and that synthesis *in situ* could account

for the higher amounts of phospholipid present in the atheromatous aorta.

It has been shown by Van Deenen and co-workers (Van Den Bosch et al., 1968; 1969) that the replacement of an unsaturated by a saturated fatty acid influences the physical characteristics of the phospholipid into which it is incorporated and maintains the physical properties of the phospholipid molecule between certain limits. Data on liquid crystals and synthetic membranes support the hypothesis that the properties of membranes are dependent on the physical characteristics of the fatty acid composition of the phospholipids (Jones et al., 1969; Pandey et al., 1968; Demel et al., 1972). Van Deenen and co-workers (DeKruyff et al., 1973) recently incorporated elaidic instead of oleic acid into the phospholipids of *A. laidlawii*. They noted a difference in the energy contents of the phase transitions of the isolated lipids which they believed may have significance to the liquid crystalline state as cholesterol was shown to preferentially interact with lipids which are in the liquid crystalline state. As phospholipids are important components in the cell membranes that make up the myocardium and the intima, the fatty acid composition of these phospholipids may be important to the rate at which lipid infiltration can occur through the cell membrane. It seems important to study their role in the step by step biochemical changes in the subcellular fractions of involved and uninvolved aortic tissue. Furthermore, these changes should be correlated with the biophysical properties of cell membranes and with the changes in pathology that have been noted at the cellular level. Such a correlation has been difficult to date as a visual inspection of an aorta cannot differentiate between the involved lipid-laden areas and the noninvolved or lipid-free areas during the initial stages in the development of atherosclerosis. The presently accepted method of staining of the aorta with Sudan IV extracts a portion of the lipid and inactivates the enzymes in the aorta. We have found that the spraying of the freshly excised aorta with a solution of Rhodamine G and visualization under ultraviolet light provide for a good means of differentiation between the involved

and noninvolved areas (Cho and Kummerow, 1974).

POSSIBLE ROLE OF THE FOOD INDUSTRY IN THE NUTRITIONAL PERSPECTIVE IN ATHEROSCLEROSIS

THE FOOD INDUSTRY has the technology to provide new food items which may reduce the risk of developing CHD. However, to do so will require information in at least four areas:

- (1) The level of total visible fat intake that will minimize the nutritional perspective of dietary fat in atherosclerosis;
- (2) The ideal percentage of PUFA in such dietary fats;
- (3) The percentage of PUFA than can be present in the trans form in shortening, margarine and salad oils; and
- (4) The possible role of cholesterol-containing food items in the development of atherosclerosis.

Level of total visible fat intake that will minimize the nutritional perspective of dietary fat in atherosclerosis

Both the American Medical Association and the National Research Council have recommended that the percentage level of fat intake should be reduced. However, such a recommendation may not be nutritionally sound as it may only increase the consumption of carbohydrate. The extra calories from carbohydrates are readily converted to saturated fatty acids or the unsaturated $\omega 9$ series of fatty acids which do not have the same biological function as the $\omega 6$ series of polyunsaturated fatty acid. As fat calories have more satiety value and are less expensive than an equivalent amount of calories from carbohydrates, it would be more economical to stay at our present percentage level of total fat and decrease the number of calories while maintaining a "well balanced" diet. However, if the level of protein intake is reduced, the level of intake of high fat food items should be reduced.

The classical nutrition studies at INCAP has shown that fat calories prevent a biological "waste" of the more expensive protein calories. In the development of substitute protein food items, it would be desirable to add enough fat calories to prevent their deamination and assure their full utilization.

Ideal percentage of PUFA in food items

The human diet contains a mixture of dietary fats that presumably supply an adequate amount of linoleic acid, yet human adrenal cholesterol esters contain the elongated (n-9) series of fatty acids which may indicate the presence of less than an optimum level of dietary (n-6) fatty acids (Table 1). The percentage of total (n-9) polyunsaturated C_{18} and C_{20} fatty acids in the human adrenal (Raggatt

et al., 1972) was in the same approximate range as found in rats fed 20% of a PUFA-free hydrogenated soybean oil and 2% corn oil or 8 and 14%, respectively. The adrenal cholesterol esters from rats fed only corn oil contained 3%, while those fed only hydrogenated soybean oil contained 34% of the (n-9) fatty acids. The total (n-6) fatty acids of human adrenal lipids was comparable in amount to that found in rats fed 2% corn oil. The hearts from rats fed 20% hydrogenated soybean oil contained significantly more total lipid than the hearts from rats (Egwin and Kummerow, 1972a) fed 20% beef tallow. An analysis of the lipids extracted from the adrenal glands, liver, heart and the erythrocytes of rats fed an adequate amount of linoleic acid ($C_{18}:2\omega 6$) has indicated that these tissue contain a substantial amount of elongated C_{20} and C_{22} PUFA fatty acids which retained the (n-6) configuration. Diets rich in linoleate, corn oil, or nutritionally adequate with respect to linoleic acid, milk fat or beef tallow, lead to an elevated level of (n-6) long chain unsaturated fatty acids in the cholesteryl esters and phospholipids in adrenal, heart and liver tissue (Egwin and Kummerow, 1972b) (Table 2). The presence of the 5% of vaccenic

acid (18:1) (n-11) in butterfat did not interfere with the accumulation of C_{20} and C_{22} PUFA acids. The percentage of PUFA in butterfat or beef tallow could be increased by the addition of corn or cottonseed oil. However, an increase in PUFA could best be obtained by increasing the PUFA content of shortenings and margarines.

Percentage of PUFA that can be present in the trans form in shortenings, margarines and salad oils

Americans consumed approximately ten billion pounds of "visible" fats per year. The major source of fat has been listed as 6.3 billion pounds of soybean oil which was converted to baking or frying fats, salad oils or margarines. The stabilization of soybean oil towards autoxidation (rancidity) by means of hydrogenation has made it possible to supply an abundance of economical and sensory acceptable calories to the American diet. In commercial practice, the undesirable linolenic acid in the soybean oil is converted to the more stable monoenoic (oleic) and saturated fatty acids through hydrogenation of the double bonds. In this process, the double bonds are also isomerized and as much as 50-60% of them are converted from the natural cis to trans forms. Stick margarine contains from 25-35%, tub margarines 15-25%, shortenings 20-30% and salad oils contain from 0-15% trans fatty acids. Household Consumption Data (USDA, 1971) indicate that margarine represents 7%, shortenings 13.2% and cooking and salad oils 12.4% of the visible fat intake. On this basis, the total trans fatty acid intake from visible fat is approximately 8%.

Does the 8% of total trans fatty acids in the diet have any nutritional or biological consequences? Such a question may be considered from both a structural and a functional parameter. The structure parameter is complicated by the interplay between the trans fatty acids and the es-

Table 1—Composition of adrenal cholesterol esters^a

Obtained from rats fed:	Total polyunsaturated fatty acids: $C_{18} + C_{20}$	
	% Amount	
	$\omega 6$	$\omega 9$
20% Hydrogenated fat	3.4	34.2
20% Hydrogenated fat + 2% corn oil	9.1	14.2
20% Corn oil	29.5	3.0
Human ^b	24.9	8.3
Human ^c	7.0	4.9

^a J. Nutr. 101: 315 (1971)

^b Lipids 5: 743 (1970)

^c Lipids 7: 474 (1972)

Table 2—Concentration of total $\omega 9$ and $\omega 6$ fatty acids (C_{18} and greater) of heart phospholipids^a

Diets	15 wk		20 wk	
	$\omega 9$	$\omega 6$	$\omega 9$	$\omega 6$
Corn oil	—	30.3	—	23.6
Milk fat	—	3.1	—	32.0
Beef tallow	1.5	5.2	4.9	31.6
Hydrog. fat	5.2	4.6	3.3	17.8
Fat-free	20.7	—	22.4	12.8

^a Results are summation of total $\omega 9$ and $\omega 6$ fatty acids, respectively, expressed as percent of total fatty acids [J. Lipid Res. 13: 500 (1972)].

Table 3-Summary data on ten groups of swine fed the basal diet plus various fat and cholesterol supplements

Diet	Total serum lipid mg%	Serum cholesterol mg%	RBC L/O	Intima cholesterol mg/g	Atherosclerosis ^b %	Lesions ^c
Basal	273 ± 12	95 ± 5	0.9	8.6	6.0	3(10)
+20% Beef tallow	331 ± 13	124 ± 5	0.6	8.0	5.2	1(11)
+20% Rearranged fat	342 ± 19	125 ± 8	2.3	8.9	3.8	0(11)
+20% Corn oil	276 ± 21	104 ± 7	2.4	9.0	5.0	2(12)
+10% Used fat and sugar	362 ± 26	131 ± 11	0.8	9.6	8.6	3(12)
+20% trans fat	388 ± 20	138 ± 9	0.7	10.4	10.0	7(12)
+20% Butterfat	332 ± 15	120 ± 7	1.0	7.2	7.3	2(9)
+Whole egg powder	303 ± 14	112 ± 5	0.8	7.7	4.8	1(11)
+Egg yolk powder	286 ± 13	98 ± 5	1.0	7.2	4.2	0(12)
+Crystalline cholesterol	245 ± 19	93 ± 3	1.3	9.1	5.2	2(12)

^a Basal-1,745 lb ground yellow corn, 200 lb soybean meal, 55 lb lysine supplement, vitamin-mineral premix, egg powder fed at cholesterol equivalent of 500 mg/day/200 lb animal weight.

^b Atherosclerosis-% of total area of aorta

^c Lesions-number raised plaques.

sential $\omega 6$ series of PUFA. We are indebted to Klenk (1965), Stoffel and Ahrens (1959), Lands et al. (1966), Privett and Blank (1964), De Tomas et al. (1963), Mohrhauer and Holman (1963), Sgoutas (1968, 1970) and Sgoutas and Kummerow (1969, 1970) for unraveling this interplay. Briefly, these workers have shown that in the absence of dietary trans fatty acids the $\omega 6$ series of PUFA esterify the β position of phosphatidylcholine and that in the absence of dietary sources of the $\omega 6$ series of fatty acids, the elongated $\omega 9$ series of fatty acids esterify this position. The trans fatty acids esterify the α position in the presence of dietary $\omega 6$ PUFA. However, in the absence of dietary $\omega 6$ PUFA, the elongated trans fatty acid esterifies the β position. The PUFA in the β position of phosphatidylcholine esterifies cholesterol. The interplay between the esterification and hydrolysis of the cholesterol esters is very precise. The elongated $\omega 6$ PUFA preferentially esterifies cholesterol and is also preferentially hydrolyzed (Goller et al., 1970). However, in the absence of elongated $\omega 6$ PUFA, the $\omega 9$ series of fatty acids esterify cholesterol. In the presence of trans fatty acids, the $\omega 6$ PUFA preferentially esterifies cholesterol; however, the trans fatty acids also esterify cholesterol. Once esterified, $\omega 6$ cholesterol esters are preferentially hydrolyzed which can result in the accumulation of cholesterol esters of the elongated $\omega 9$ fatty acids in the tissue.

In a recent study in our laboratory (Mizuguchi et al., 1974), 6-month old swine were fed a commercially available hydrogenated fat which contained less than 1% C18:2 and 40% trans fatty acids in its mixed fatty acid composition (Table 3). The 6-month old swine were fed for 8 months 10 or 20% of the hydrogenated fat in addition to a diet which

contained all of the essential minerals and vitamins; this basal diet furnished the equivalent of 14.3% protein and 3% corn oil. Other groups of swine were fed tallow, corn oil, used fat, butterfat, egg yolk, whole egg powder or crystalline cholesterol equivalent to 2 eggs/200 lb animal weight.

The results indicated that the total lipids in the hearts of swine fed hydrogenated fat contained approximately 9% elaidate after 8 months on the diet. The plasma lipids contained approximately 5.6% elaidate in the cholesterol esters, 4.3% in the triglyceride and 12.3% in the phospholipid fraction, respectively. As would be expected, the LDL and HDL fraction of plasma lipoproteins from swine fed hydrogenated fat contained more lipid than those on the basal diet.

The total plasma lipid level was higher in swine fed the "trans" fat than in those fed tallow, non-trans hydrogenated fat or corn oil and the plasma cholesterol level was higher than the cholesterol level in plasma from swine fed diets which contained cholesterol. The serum cholesterol level was also elevated in the swine fed beef tallow or butterfat. However, it was not elevated in swine fed egg yolk, whole egg or crystalline cholesterol at a level equivalent to 2 eggs/day/200 lb of animal weight. Supplementation with corn oil resulted in lower serum cholesterol levels than supplementation with beef tallow or butterfat. However, supplementation with rearranged fat stimulated approximately the same response as corn oil. The rearranged fat was prepared from completely hydrogenated soybean oil and cottonseed oil.

In agreement with the conclusions of the National Diet Heart Study (1968), the present results indicated that the L/O ratio of the lipids in the erythrocytes was

higher when corn oil rather than when "hard" fats such as butterfat or tallow served as a dietary fat. Furthermore, the C20:4 $\omega 6$ level of the erythrocytes from those fed trans fat was lower than in swine fed the other dietary fats. Although the presence of trans fatty acids in the dietary fat decreased the amount of linoleic acid in the lipids of the erythrocytes, the L/O ratio of these lipids was higher than the L/O ratio of the lipids obtained from human erythrocytes in the Nation Heart Study. The L/O ratio has been used as an index of adherence to a high PUFA diet. The present study indicated that a high L/O ratio dietary fat will lower serum cholesterol levels and it has been assumed that the L/O ratio of a dietary fat influenced the degree of atherosclerosis (National Diet Heart Study, 1968). However, such an assumption cannot be proven with human experimental subjects. Furthermore, these parameters were of no value in predicting whether raised plaques or fatty streaks had developed in the arteries.

The normal intima obtained from all ten groups showed a similar concentration of total lipid and lipid classes. The total lipid content of the involved intima was increased about 70% or as much as 42.5 mg/g tissue. The highest concentration of cholesterol was noted in the swine fed trans fat or 10.4 mg/g tissue. However, the involved intima from all ten groups did not show statistically significant differences in concentration of total lipid, cholesterol and other lipids. Both the normal and the involved intima did not show significant differences when compared to the proportion of each lipid class to the total lipid.

Fatty streaks were observed in all thoracic and abdominal aorta, whereas raised lesions were observed around the

terminal portion of the abdominal aorta and the orifices of celiac and renal arteries. The swine fed trans fat had the largest amount of atherosclerosis or 10% of involvement. The aorta of 7 out of 12 swine fed trans fat had raised lesions (58.3%), whereas raised lesions were observed in only 14 out of 100 swine fed the other diets (14%). The aortas from those fed the 10% used fat and sugar had the second largest amount or 8.6% of involvement.

The high calorie to protein ratio of the dietary fat as well as other yet unknown dietary variables may have contributed to the susceptibility of these swine to the development of atherosclerosis. Furthermore, the presence of a high percentage of trans fatty acids in a dietary fat may require the presence of more than 2-3% linoleic acid to preserve the integrity of the $\omega 6$ phospholipids in the cell membrane of the smooth muscle cells in the intima. The hydrogenated fat that was used in this study contained less than 1% linoleic acid and between 40-50% trans fatty acids. In two separate studies, Zalewski and Kummerow (1968) and Carpenter and Slover (1973), commercial margarines were found to contain from 3-43% linoleic acid and from 15-54% trans fatty acids.

The level of dietary linoleic acid in a fat which contains "elaidinized" fat, that is, trans fatty acids may be important to atherogenesis. It was shown by McMillan and co-workers (1963) that a higher serum cholesterol level and more atherosclerosis occurred in rabbits fed elaidinized olive oil than in those fed olive oil. However, such differences were not found significant in rabbits fed elaidinized linoleic acid which contained 18% cis-cis linoleic acid (Weigensberg and McMillan, 1964). More PUFA may be necessary when consumed with sources of trans fatty acids. In fact, previous studies have shown that a greater percentage of trans fatty acids are incorporated into tissue in the presence than in the absence of linoleic acid (Johnston et al., 1958). The inclusion of 2% dietary linoleic acid in a high trans hydrogenated fat diet facilitated incorporation of elaidic acid in adipose tissue, triglycerides, cholesterol esters and phospholipid fractions. The increases were approximately 10% in adipose tissue, 4% for triglycerides, 5% for cholesterol esters and variable in phospholipids (Sgoutas et al., 1973).

The percentage of elaidinized or trans fatty acids in a culinary fat seemed to determine the degree of response in human subjects. When fed as 40% of total calories, a hydrogenated fat which contained 35% trans fatty acids increased serum cholesterol level (Vergosen, 1972) but one which contained 10% of trans fatty acids had no elevating effect on serum cholesterol levels (Erickson et al.,

Table 4—Concentration of elaidate in lipid classes of human as compared with swine plasma

	Swine ^a	Human
Triglycerides	4.3%	2.1-6.7%
Phospholipids	12.3%	3.1-5.7%
Cholesterol Esters	5.6%	1.7-5.1%

^a Fed 20% hydrogenated fat (40-50% trans) for 8 months

1964). The triglycerides, cholesterol esters and phospholipids in human serum contained approximately the same level of trans fatty acids as 6 months old swine which had been fed for 8 months a hydrogenated fat which contained 40% trans fatty acids (Kummerow et al., 1973) (Table 4). The red blood cells from these subjects contained from 0 to 5.3% trans fatty acids and had an L/O ratio of 0.4 to 1.0. Human tissue contains trans fatty acids (Johnston et al., 1958): approximately 2.4-12.2% in adipose tissue, 4-14% in liver, 4.6-9.3% in heart and 2.3-8.8% in the aorta.

It is possible that the percentage of cis and trans isomers as well as the amount of PUFA in a culinary fat may be important to its possible role in the development of atherosclerosis. This role cannot be studied in man as effectively as in swine as an animal model. I believe that such a study should be carried out with commercially available hydrogenated fats containing various levels of cis-cis linoleic acid. The results to date indicate that a trans-free hydrogenated fat may maximize the biological worth of the $\omega 6$ series of PUFA (Lands et al., 1966; Privett and Blank, 1964; Lands, 1965).

Possible role of cholesterol-containing food items in the development of atherosclerosis

To date, the choice of food items which contain protein has been governed by consumer preference for animal protein sources and by individual taste. As animal proteins become more expensive and less are consumed, the biological worth of substitute protein sources becomes increasingly more important and food intake governed solely by taste will become more critical. It may have been possible to indulge in the consumption of empty calories (soft drinks and potato chips) on the present high level of animal protein intake. However, if this level of animal protein intake is reduced to a crucial level, two developments seem necessary: (1) to make available substitute food items equivalent to animal protein in nutritional value; and (2) either to remove the source of empty calories from the diet or to enhance their food value by the addition of essential nutrients. The

food industry can increase its efforts to reach these goals so that we will not be caught in a nutritional crisis which will have much more serious consequences to our health and well being than the energy crisis. To date, the complete protein that is produced by beef cattle and dairy cows from marginal grasslands has been more economical to produce than substitute proteins. Animal protein will continue to serve as a substantial source of protein as only 30% of our agricultural lands yield crops which can be processed into foods for direct human consumption (USDA, 1973). If the practice of "finishing" 700-lb grassland beef with corn is abandoned, the amount of beef available at the supermarket will be cut to half of what is presently available. Furthermore, as grass-fed beef is too "tough" to use as roasts and steaks, it will have to be consumed as ground meat. A study on the ideal balance between direct and indirect consumption of cereal grains, therefore, seems necessary in order to use our grassland at maximum efficiency (Hegsted, 1974).

The development of cholesterol-free protein sources cannot be based on food composition data alone; it must be based on nutritional value as biological need is more important than technological expediency. In its attempt to comply with the recommendations of the American Medical Association and the National Research Council, segments of the food industry has provided a nutritionally inferior product. The nutritionally inferior product is in the form of a cholesterol-free substitute for shell eggs.

The cholesterol-free egg substitute contains, according to the label on the carton, "egg white, corn oil, nonfat dry milk, emulsifiers (vegetable lecithin, mono and diglycerides and propylene glycol monostearate), cellulose and xanthan gums, trisodium and triethyl citrate, artificial flavor, aluminum sulfate, iron phosphate, artificial color, thiamin, riboflavin and vitamin D" (Table 5). A comparison of the nutrients in 100g of Egg Beaters on Second Nature egg substitute with the nutrients in 100g of "farm fresh eggs" indicates a list of nutrients which should be able to meet the growth requirements of weanling rats (Navidi and Kummerow, 1974). However, the pups from the mothers fed Egg Beaters averaged 31.6g and those fed whole egg averaged 66.5g in weight at 3 wk of age as compared to 70g for pups from those fed Purina Laboratory Chow. Both the mothers and pups fed Egg Beaters developed diarrhea within 1 wk; those fed whole egg did not develop diarrhea. The pups fed the egg mixtures were weaned at 5 wk of age. All of those fed Egg Beaters died within 3-4 wk after weaning. The general appearance of the rats fed Egg Beaters indicated a gross deficiency in one or

Table 5—Comparison of nutrients in Egg Beaters or shell eggs with nutrient requirements of growing rats

Nutrients	100g of Egg Beater	100g of Egg	Requirement of growing Rat—% Diet ^a
Protein	11g	12.8g	13.3g
Fat	12.5g	11.4g	5.5g
Calories	166.66	160	GE/day 76 for each rat (444 Kcal/100g).
Ca	81.6 mg	54 mg	560 mg
P	71 mg	204 mg	440 mg
Na	181 mg	122 mg	60 mg
K	213 mg	128 mg	200 mg
Iron	1.8 mg	2.2 mg	38.9 mg
Cholesterol	<1.6 mg	550 mg	—
Vitamin A	1350 I.U.	1180 I.U.	0.67 mg (retinol/kg)
Vitamin D	43 I.U.	50 I.U.	111.1 (I.U./Kg)
Thiamine	0.13 mg	0.1 mg	0.14 mg
Riboflavin	0.43 mg	0.3 mg	0.28 mg
Choline chloride	b	582 mg	83.3 mg/100g
Ca pantothenate	b	2.7 mg	0.89 mg/100g
Vitamin B ₆	b	0.3 mg	0.78 mg/100g
Vitamin B ₁₂	b	0.001 mg	0.00056 mg/100g
Biotin	b	0.04 mg	0.1 mg/100g

^a "Nutrient Requirements of Laboratory Animals." No. 10, 2nd ed., 1972. National Academy of Sciences, Washington, D.C.

^b Not listed

more nutritional factors as compared to those fed whole egg. As the animals had a tendency to become coated with the Egg Beaters, the animals were washed gently with a mild detergent solution and dried with paper towels. The washing removed some of the hair as well as the Egg Beaters.

Neither Egg Beaters nor shell eggs serve as a single food source in the human diet. Furthermore, both Egg Beaters and shell eggs are subjected to heat treatment and are not consumed in the raw state. The rat pups were weaned at 5 instead of the usual 3 wk in order to provide the advantage of rat milk supplementation for them. However, it is evident that shell eggs, which contain the lipotropic-laden egg yolk, furnish one or more nutritional factors which are absent in Egg Beaters. These nutritional factors are no doubt present in the common food items which comprise the diet of human adults and could probably be added to the Egg Beaters formulation. However, these nutritional factors may not be present in adequate amounts for infants fed milk and Egg Beaters instead of egg yolk from a soft boiled egg. The Council statement (AMA, 1972) under point (3) should be considered and "care be taken to assure that the dietary advice given does not compromise the intake of essential nutrients." This statement should also be considered in the quest of food items free of cholesterol in the diets of infants. Furthermore, the assumption that the consumption of eggs, meat and dairy products by growing children should be

minimized and replaced with PUFA may result in nutritional disaster (Fredrickson and Levy, 1971). The protein calorie-ratio is important to rapid growth in farm animals and poultry and deserves further study in man in the development of new food items.

SUMMARY

IT SEEMS EVIDENT that dietary advice should take into consideration the availability of food items, their composition and their subtle impact on the nutrition and the biochemistry of the individual cell. The food industry has a vital role to play in furnishing new food items which have been thoroughly tested for more than their freedom from toxic compounds. New food items should be considered in terms of their total nutritional impact as such food items will become increasingly more important to human welfare in a world of rapidly shrinking supplies of food items which have served as the main sources of proteins, vitamins and minerals for countless generations.

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THE INFLUENCE OF EGG CONSUMPTION ON THE SERUM CHOLESTEROL LEVEL IN HUMAN SUBJECTS

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Abstract: The influence of whole fresh eggs on the serum cholesterol level in men and women was studied independently in hospitalized patients in Sofia, Prague and Urbana-Champaign. The patients were fed two eggs or the equivalent of two eggs in a custard base or milk shake in addition to the foods that were consumed in their diet pattern. The serum cholesterol level was determined before and at periods varying from 5 hr. to 54 days after the consumption of the eggs. The mixed fatty acid composition of the total lipids in the serum and the erythrocytes was also determined. In the majority of patients, the serum cholesterol level did not change significantly 5 hr. after the consumption of 465 mg of cholesterol in an egg custard base or milk shake or after up to 54 days of continued consumption of two whole eggs per day. The serum cholesterol level of some subjects increased and others decreased at all three experimental sites. A comparison of the mixed fatty acid composition of the total serum lipids obtained from men and women who had received treatment for other reasons than cardiovascular disease with those that had been treated for cardiovascular disease indicated that the serum from both groups contained a substantial amount of polyunsaturated fatty acids. The lipids extracted from the red blood cells obtained from patients in Urbana-Champaign and Sofia did not differ significantly in linoleic and arachidonic acid content. *Am. J. Clin. Nutr.* 30 : 000-000, 1977.

A low saturated fat/low cholesterol diet has been recommended as one of the most effective means of controlling serum cholesterol levels [1]. As an egg contains a relatively large amount of cholesterol (approximately 250 mg/100 g), less consumption of eggs has been suggested [2-4] as a means of lowering serum cholesterol levels. However, a decreased per capita consumption of 123 eggs since 1945 [5] has not decreased the total daily cholesterol intake in the United States as the per capita consumption of meat and dairy products has increased. Calculations based on per capita food consumption data since 1909, the date such information first became available [6], and the cholesterol content of the individual food item [7], indicate that the total daily cholesterol intake as furnished by meat, dairy products, and eggs equaled 545 mg in 1909, 614 mg in 1960, 602 mg in 1965, and 600 mg in 1973 (Table 1). Furthermore, because of an increased consumption of chicken fat, which contains six times more linoleic acid than beef fat [8], the composite mixture of "invisible" fat in animal food products actually supplied 0.7 pounds more linoleic acid/capita per year to the diet in 1975 than it did in 1909.

The composite mixture of "visible" fats in the American diet has also changed in composition. In 1909, lard, beef tallow, and butterfat

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furnished the main source of culinary fat; a portion of the beef tallow was mixed or compounded with cottonseed oil and sold as margarine. Shortenings made from hydrogenated vegetable oils did not become available until 1911 [9], and the ratio of the consumption of animal to vegetable fats has continued to change at an accelerated rate since that date. For example, the intake of visible animal fats has decreased from 21.9 in 1950 to 10.2 pounds/capita per year in 1975 and the intake of vegetable fat has increased from 24.0 to 43.1 pounds during the same time period [10]. Approximately two thirds of these 43 pounds of vegetable fat was hydrogenated or converted to a "saturated" fat in order to stabilize it against oxidation.

As many epidemiological studies have provided valuable data [11-18], it seemed of interest to compare serum cholesterol levels of Americans with those of Czechs or Bulgarians who have not substantially increased their per capita hydrogenated fat intake but have increased their per capita egg intake. The consumption of eggs has increased from 248 to 301 in Czechoslovakia and from 127 to 163 in Bulgaria (R. E. Anderson, Jr., personal communication, Foreign Commodity Analysis, USDA, Washington, D.C.) and has decreased from 314 to 279 in the United States from 1971 to 1975 [5]. In the present study, the effect of eggs on convalescent patients from three local hospitals in Urbana-Champaign was compared to the effect of eggs on similar patient groups in Prague and Sofia.

MATERIAL AND METHODS

In Urbana, two groups of human subjects were used: a group of 30 randomly selected volunteer hospital patients suffering from cardiovascular disease and a group of 30 randomly selected volunteers in the hospital for reasons other than cardiovascular disease. The latter group did not include patients with diabetes, obesity, liver disease, intestinal problems, or lipid abnormalities. Blood samples, 5 ml, were taken before breakfast at 8:30 AM and again after breakfast at 11:30 AM. The dietary source of cholesterol was then consumed and a 5 ml blood sample was taken at 4:30 PM. Whole pasteurized eggs in a flavored milk shake or mixed with a custard base was used as a source of cholesterol. The custard was prepared from 1 cup (6 ounces) custard base (Delmark Quick Egg Custard Mix, Delmont Co., Minneapolis, Minn.) and $4\frac{3}{4}$ cups skim milk; $4\frac{2}{3}$ ounces of this mix, and $3\frac{1}{3}$ ounces of whole pasteurized eggs (Gerber Products Co., Fremont, Mich.) were blended together, chilled, and served to provide 465 mg of cholesterol in each serving. The milk shake contained an equivalent amount of cholesterol. The hospital menu of 1,990 cal contained 78 g of protein, 94 g of fat, and 208 g of carbohydrate with a minimum of 340 cal from skim milk, 200 cal from bread or cereals, 135 cal from margarine, 150 cal from fruits or vegetables, and 4 ounces of lean meat/day in addition to the flavored milk shake or custard. Cholesterol determinations were carried out according to the method of Zak et al. [19]. The mixed fatty acid composition of the total lipids in the serum and in the erythrocytes was determined as previously described [20, 21]. The chloroform-methanol that was used to extract the lipid contained 0.01% α -tocopherol; all manipulations were carried out under nitrogen.

In Prague, a group of 21 patients who had been hospitalized for at least 1 week was used. No patients with malignancies, cardiac decompensation, unstable angina pectoris, or postoperative status were included. The diet was prepared in the metabolic kitchen from commonly used food components in Prague. It furnished daily 250 mg of cholesterol and $2,400 \pm 180$ cal of which 40% was supplied by fat. The fat contained 42.5% polyunsaturated fatty acid, 32.5% monounsaturated, and 25% saturated fatty acids. The cholesterol was furnished by the blending of two fresh eggs into a soup that was provided as part of the midday meal; less than one kilo of fluctuation in weight of the average patient was noted during the hospital stay. Blood samples were obtained after at least a 12-hr fast. The serum cholesterol and triglyceride levels were determined according to the method of Grafnetter et al. [22, 23] and lipoprotein phenotyping was determined by electrophoresis [24].

In Sofia, two groups each of twenty patients who had been operated on for inborn or acquired heart defects were fed a diet of 2,330 cal in four meals consisting of: 96 g of protein, 77 g of fat, and 295 g of carbohydrate. The protein was supplied as beef or chicken, the fat as sunflower oil, and the carbohydrate as bread, high starchy foods or desserts. No hydrogenated vegetable fat was used in these food items as such fats are not available in Bulgaria. Two whole eggs were added at lunch to the patients on this convalescent diet. Three milliliters of blood were drawn after a 12- to 14-hr fast and the serum cholesterol assayed according to the method of Watson [25]. The total lipid level of the serum was determined photometrically [26]. The percentage composition and cholesterol content of the three basal diets is listed in Table 2.

RESULTS

In the majority of patients, the serum cholesterol level did not change significantly either after 5 hr or after up to 54 days of continued consumption of two whole eggs or 465 mg of cholesterol in an egg custard base or milk shake. In Sofia, the average serum cholesterol of 231 ± 56 mg/100 ml remained unchanged and the total serum lipid level increased from 778 ± 232 mg/100 ml to 819 ± 225 mg/100 ml in 20 patients fed the convalescent diet for a period of time which varied from 20 to 39 days (Table 3). The serum cholesterol level increased from 261 ± 57 mg/100 ml to 266 ± 56 mg/100 ml and the total lipid level decreased from 856 ± 287 mg/100 ml to 853 ± 269 mg/100 ml in 20 patients fed two eggs/day in addition to the same convalescent diet for a period of time which varied from 20 to 54 days. The serum cholesterol and total serum lipid levels increased in some patients and decreased in others; the serum cholesterol level in one patient in each group changed by more than 100 mg/100 ml.

In Prague, the average serum cholesterol level decreased from 273 ± 56 mg/100 ml to 251 ± 53 mg/100 ml and the triglyceride levels increased from 173 ± 104 mg/100 ml to 185 ± 169 mg/100 ml in the 21 patients fed the convalescent diet for 7 days (Table 4). As in Sofia, when these patients were fed 2 eggs/day for 7 days, in addition to the convalescent diet, the serum cholesterol level increased in some patients and decreased in others. The serum cholesterol level increased an average of 2 mg/100 ml or from 251 ± 53 mg/100 ml to 253 ± 52 mg/100

ml and the triglyceride level increased from 185 ± 169 ml/100 ml to 220 ± 203 mg/100 ml. No apparent relationship was noted between the response to eggs and the lipoprotein phenotype.

In Urbana, the serum cholesterol level of only four out of 60 subjects changed more than 20 mg/100 ml 5 hr after the consumption of eggs in addition to the regular diet (Table 5). The serum cholesterol level of 15 men hospitalized for reasons other than cardiovascular disease increased an average of 7 mg/100 ml and of 15 women decreased an average of 3 mg/100 ml or from 174 and 228 mg/100 ml before to 181 and 225 mg/100 ml, respectively, 5 hr after the consumption of an amount of cholesterol equivalent to two eggs. Similar results were obtained with the patients suffering from cardiovascular disease. In this somewhat older group of patients, the serum cholesterol level of 15 men increased an average of 7 mg/100 ml and of 15 women decreased an average of 11 mg/100 ml or 182 to 189 and 197 to 188 mg/100 ml, respectively, after the consumption of an amount of cholesterol equivalent to two eggs. As no significant differences in serum cholesterol levels were noted between samples taken at 8:30 and 11:30 AM, only the values at 11:30 AM were listed in Table 5.

A comparison of the mixed fatty acid composition of the total serum lipids obtained in Urbana-Champaign from the patients who had received treatment for other than cardiovascular disease with those that had been treated for cardiovascular disease indicated that the serum from both groups contained a substantial amount of polyunsaturated fatty acids. The serum obtained from convalescent noncardiovascular men contained $22 \pm 2\%$ linoleic, $0.5 \pm 0.3\%$ eicosatrienoic, and $3 \pm 0.5\%$ arachidonic acid (Table 5). The fatty acid profile in the noncardiovascular women or the men and women cardiovascular patients did not differ significantly from these values. The lipids extracted from the red blood cells from these four groups of patients also did not differ significantly. They contained more arachidonic and palmitic and less linoleic acid than the serum. The lipids extracted from the red blood cells contained $19.6 \pm 0.2\%$ linoleic, $4.2 \pm 0.5\%$ arachidonic, $0.5 \pm 0.5\%$ eicosatrienoic, $26.6 \pm 1.9\%$ oleic, $13.0 \pm 0.2\%$ stearic, and $35.4 \pm 2.9\%$ palmitic acid. In Sofia, the lipids extracted from a solid to a liquid diet [29], a change in dietary fatty acid contained $11.3 \pm 2.1\%$ linoleic and $7.9 \pm 2.7\%$ arachidonic acid and those from eleven hyperlipemic patients contained $6.2 \pm 1.6\%$ linoleic and $4.5 \pm 1.4\%$ arachidonic acid.

DISCUSSION

The nutritionally complete diets that were used in Sofia, Prague, and Urbana-Champaign may be the explanation for the insignificant changes in serum cholesterol levels that were noted after the consumption of an amount of cholesterol equivalent to two eggs/day. All of the dietary components had been a regular part of the diet and did not introduce variables known to influence serum cholesterol levels such as a lack of fiber [27], a change in nutrient bulk [28], a change from a solid to a liquid diet [29], a change in dietary fatty acid composition [30], or an excessive level of dietary fat [31]. Furthermore, unlike previous studies [29, 31-34], whole eggs rather than egg yolk powder or crystalline cholesterol were used in the present study. Egg yolk powder contains more cholesterol than whole egg powder or

3960 and 2400 mg/100 g, respectively [7.] Egg yolk powder is therefore a more concentrated source of dietary cholesterol than whole egg powder for experimental studies. However, whole eggs rather than egg yolk are normally used in meal preparation. The egg yolk in two medium sized fresh eggs furnishes only 5.4 g of protein as compared with 11.7 g of protein for the whole egg (Table 6). Even though two medium sized fresh whole eggs contain only 11.7 g of protein, they contain, except for methionine and phenylalanine, the approximate total daily requirement for all eight of the essential amino acids [35]. Two fresh egg yolks do not provide enough protein to satisfy the total daily amino acid need for any of the eight essential amino acids, although two fresh egg yolks contain as much cholesterol as two fresh whole eggs [36]. In spite of the presence of other sources of protein [29-34], someone eating two whole eggs/day would be less likely to be deficient in any of the essential amino acids than someone eating egg yolk.

Amino acids are essential for the building of the apolipoproteins which "carry" the cholesterol in the blood [37, 38]. An arginine-rich apoprotein has been found in the serum of patients with type III hyperlipoproteinemia and in animals fed an excessive amount of cholesterol [39]. This arginine-rich apoprotein has more nonpolar and polar groups capable of combining with more cholesterol and phospholipid than normal apolipoprotein [38] and therefore increases serum cholesterol levels. It has also been shown in previous studies [40-42] that a balance dietary amino acid level resulted in a lower serum cholesterol level than an imbalanced amino acid level [43]. For example, chicks kept for 7 days on a diet containing synthetic amino acids plus 1.38%, 1.74%, or 2.82% arginine had serum cholesterol levels of 120, 103, and 125 mg/100 ml, respectively. Similar differences in serum cholesterol levels were noted after the deletion or excess addition of serine, alanine, leucine, lysine, proline, or methionine. The serum cholesterol level may, therefore, be as dependent on the amount and quality of dietary protein as on the source and dietary cholesterol levels that have been used in previous experimental designs [29, 31-33]. None of these experimental designs recognized that the results obtained with egg yolk powder do not necessarily reflect the results that might have been obtained with whole eggs and should, therefore, not be projected to diet recommendations for human subjects [1-5]. A recent study with whole eggs corroborated this viewpoint [44].

Haganfeldt et al. [45] have reported that patients who had suffered a myocardial infarction had lower concentrations of free octadecatrienoic and arachidonic acids and a higher concentration of eicosatrienoic acid in the plasma as compared to the controls. However, these data may only indicate that the culinary fats that are used in Sweden are more deficient in linoleic acid than culinary fats that are used in the United States or Bulgaria. The subjects that were used in the present study were not deficient in linoleic acid. The linoleic acid level of the serum and erythrocyte lipids obtained from the blood of convalescent patients suffering from cardiovascular disease did not differ significantly from the patients who had received treatment for other than cardiovascular disease and was similar to the level reported in the National Diet Heart Study [3]. Variation in the mixed fatty acid composition of the total serum lipids indicated that some patients had consumed more linoleic acid than others. Although it has been

shown in numerous studies [46-48] that individual dietary fats have a quantitative effect on serum cholesterol levels, our data, and data provided by the National Diet Heart Study seems to indicate that the serum level of linoleic acid is no different in the United States than the level noted in Bulgaria (P. Ilinov, personal communication; see also Ref. 26). This observation does not preclude the possibility that the kind of polyunsaturated fatty acids in cell membranes is important to the function of such membranes [49, 50] and may be relevant to cardiovascular disease.

It would seem desirable to test the response of a particular patient before assuming that the serum cholesterol level will increase when whole eggs are included in the diet of that patient. Such a test would eliminate uncertainty and provide for a wider choice of food items than the present recommended protocol provides [1-4]. However, it may be advantageous to run more than one cholesterol determination in order to obtain reliable information on a specific subject's response to a source of dietary cholesterol. The results obtained in Sofia and in Prague as well as those noted in previous studies [29, 30, 33, 34] indicate that in some individuals a simple change in diet regime per se influences their serum cholesterol level.

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TABLE 1.—ANNUAL PER CAPITA CONSUMPTION OF ANIMAL FOOD PRODUCTS

Year	Meat		Poultry		Fish		Eggs		Dairy Products		Animal fat		Total Pounds of linoleic acid	Total cholesterol
	Pounds	Pounds of linoleic acid ¹	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Quarts	Pounds of linoleic acid	Pounds	Pounds of linoleic acid		
1909	146.6	0.70	15.9	0.38	13.9	0.47	35.1	0.63	178	0.18	12.4	0.43	2.8	545
1960	146.9	.71	34.6	.83	13.2	.45	42.5	.76	238	.24	7.5	.26	3.3	614
1961	145.9	.70	37.8	.90	13.7	.47	41.7	.75	235	.24	7.4	.26	3.3	563
1962	147.1	.71	37.4	.90	13.6	.46	41.4	.75	235	.24	7.3	.26	3.3	609
1963	152.0	.73	37.9	.91	13.7	.47	40.4	.73	234	.23	6.9	.24	3.3	610
1964	155.7	.75	38.9	.93	13.5	.46	40.4	.73	235	.24	6.9	.24	3.4	616
1965	148.3	.71	41.3	.99	13.8	.47	39.8	.72	234	.23	6.4	.22	3.3	602
1966	151.4	.73	44.3	1.1	13.9	.47	39.7	.71	234	.23	5.7	.20	3.4	607
1967	158.3	.76	46.2	1.1	13.6	.46	40.6	.73	230	.23	5.5	.20	3.5	623
1968	162.4	.78	45.8	1.1	14.0	.48	40.1	.71	231	.23	5.7	.20	3.5	628
1969	161.4	.77	47.8	1.1	14.2	.48	39.3	.71	230	.23	5.4	.19	3.5	633
1970	164.6	.79	50.1	1.2	14.8	.50	39.5	.71	226	.23	5.3	.19	3.6	628
1971	170.0	.82	50.3	1.2	14.4	.49	39.9	.72	228	.23	5.1	.18	3.6	639
1972	166.5	.80	52.5	1.3	15.3	.52	39.0	.70	228	.23	4.9	.17	3.7	631
1973	154.6	.74	50.5	1.2	15.6	.53	37.2	.67	229	.23	4.8	.17	3.5	600

¹ Calculations of pounds of linoleic acid based upon assumption that amount of linoleic acid in certain foods has not changed over the past 60 yr. (Fat Content and Composition of Animal products, The National Research Council, December, 1974).

² Milligrams per day as calculated from the total per capita intake of each food item and its cholesterol content (J. Am. Oil Chemists' Soc. 27: 414, 1950).

TABLE 2.—THE PERCENTAGE COMPOSITION, TOTAL CALORIES, AND CHOLESTEROL CONTENT OF THE 3 BASAL DIETS

	Urbana	Prague	Sofia
Protein.....	20	20	20
Fat.....	40	40	17
Carbohydrate.....	40	40	63
Total calories.....	1,990	2,400	2,330
Cholesterol (mg/day).....	600	250	¹ 600

¹ Variable, from 400 to 600 mg/day.TABLE 3.—DYNAMIC CHANGES IN MG/100 ML SERUM CHOLESTEROL AND MG/100 ML TOTAL LIPIDS OF PATIENTS IN SOFIA ON THE CONVALESCENT DIET (A) AND OF PATIENTS ¹ EATING 2 EGGS IN ADDITION TO THIS DIET (B)

Clinic number	Sex	Age	0 days		7-35 days		20-54 days 20-39 days	
			Serum cholesterol	Total lipid	Serum cholesterol	Total lipid	Serum cholesterol	Total lipid
Patients on the convalescent diet (A):								
794	F	37	270	1,150			230	720
836	F	43	210	600	250	2 780	225	600
847	F	47	360	1,150	280	930	330	1,380
902	F	50	210	810			250	840
934	F	30	245	630	250	730	140	510
936	F	57	235	690	300	1,000	215	840
975	F	29	250	880	200	960	295	
960	F	27	160	630			180	780
981	F	36	270	780	180	810	315	1,000
848	M	24	220	630	205	660	220	660
872	M	32	260	840	200	3 870	230	930
904	M	22	160	660	185	690	195	750
993	M	50	220	690			210	730
251	M	51	350	1,400			330	1,300
295	M	19	200	780			170	700
307	M	21	180	570			160	540
416	M	21	175	480			225	810
417	M	33	275	960	220	1000	280	900
438	M	25	180	630	210	690	225	900
439	M	28	180	600	200	660	190	670
Average	20	34±11	231±56	778±232	223±38	815±133	231±55	819±225
Patients on the convalescent diet plus 2 eggs/day (B):								
788	F	27	180	650	200	630	210	570
789	F	39	320	840	310	1,000	280	800
835	F	24	240	540	190	4 900	210	690
838	F	33	360	1,000	320	5 960	360	1,000
869	F	47	370	1,800			360	1,700
871	F	43	300	1,000	305	780	320	1,000
874	F	36	310	1,100	330	1,000	240	810
937	F	36	270	600	310	900	180	570
938	F	29	210	720	230	780	240	900
795	M	36	160	600	230	6 900	310	960
796	M	25	180	590	175	630	160	510
905	M	39	240	720	235	510	210	600
1024	M	32	225	690	250	840	270	840
1007	M	50	230	660	225	7 780	260	840
1471	M	51	270	1,100			300	
1466	M	40	285	960			290	
308	M	42	240	780	250	630	280	960
373	M	33	290	990	250	930	300	1,000
415	M	30	290	780	300	840	320	960
431	M	25	250	1,000	250	800	220	650
Average	20	36±8	261±57	856±287	256±48	812±143	266±56	853±269

¹ Diagnosis, atrial septal defect; ductus arteriosus persists; mitral stenosis; ventricular septal defect; stenosis arteriae pulmonalis—post operative, 28 days or more.² At day 23, cholesterol=245, total lipids=900.³ At day 17, cholesterol=210, total lipids=690.⁴ At day 19, cholesterol=230, total lipids=750.⁵ At day 21, cholesterol=350, total lipids=1,200.⁶ At day 22, cholesterol=275, total lipids=1,000.⁷ At day 45, cholesterol=225, total lipids=840.

TABLE 4.—DYNAMIC CHANGES IN SERUM CHOLESTEROL AND TRIGLYCERIDE LEVELS OF PATIENTS IN PRAGUE ON THE CONVALESCENT DIET (A) AND THE SAME PATIENTS ON THIS DIET PLUS 2 EGGS/DAY FOR ANOTHER 7 DAYS DIET (B)

		Convalescent diet (A)				Diet A+2 eggs/day (B)			
		0 days		7 days		7 days		Phenotype or diagnosis	
Sex	Age	Serum cholest- erol	Tri- glyceride	Serum cholest- erol	Tri- glyceride	Serum cholest- erol	Tri- glyceride		
Clinic number:									
86/73	M	53	282	217	278	100	242	143	HLP IV.
578/72	M	26	210	258	244	182	227	157	HLP II.
53/73	M	51	258	93	272	114	235	132	HLP II.
559/72	M	44	205	71	212	64	199	132	HLP IV.
573/72	M	52	235	121	206	153	209	132	HLP IV.
546/72	M	46	266	93	227	132	206	114	HLP IV.
556/72	M	38	287	300	258	186	261	114	HLP IV.
608/72	M	44	353	600	278	271	262	230	HLP II.
628/72	M	42	372	942	293	443	353	859	HLP IV.
652/72	M	49	276	450	276	450	227	307	HLP IV.
622/72	M	36	206	228	151	114	179	115	Asthenia.
617/72	M	51	384	164	295	86	321	67	HLP II.
605/72	F	37	375	79	384	114	356	100	HLP II.
165/73	M	57	282	243	262	184	311	184	HLP II.
184/73	M	38	256		234		261		M. Buerger.
195/73	F	47	299	205	336	205	293	177	HLP II.
423/73	F	53	258	110	205	98	241	123	Neurosis.
435/73	M	53	227	125	177	129	184	181	HLP IV.
433/73	M	47	214	135	225	154	281	91	HLP II.
462/73	F	50	234	168	250	109	273	95	Neurosis.
445/73	M	43	246	285	216	169	192	252	Duodenal ulcer.
Average----	21	46±7	273±56	173±104	251±53	185±169	253±52	220±203	

Note: HLP=Hyperlipoproteinemia.

TABLE 5.—COMPARISON OF CHOLESTEROL AND MIXED FATTY ACIDS IN SERUM LIPIDS BEFORE AND 5 HR AFTER A TEST MEAL IN URBANA¹

	Noncardiovascular		Cardiovascular	
	Male	Female	Male	Female
Average age	46±4	61±3	59±5	71±3
Serum cholesterol (0 hr) mg/100 ml	174±10	228±13	182±11	197±13
Serum cholesterol (5 hr) mg/100 ml	181±8	225±14	189±9	188±13
Serum fatty acids (0 hr) (percent):				
C14:0	1±0.2	0.6±0.1	1±0.1	2.0.7±0.1
C16:0	40±3.0	51±5.0	42±2.0	40±2.0
C16:1	2±0.3	2±0.6	2±0.3	2±0.3
C18:0	7±1.0	4±0.6	7±1.0	6±0.6
C18:1	24±2.0	19±1.0	25±2.0	24±1.0
C18:2	22±2.0	16±3.0	18±2.0	22±2.0
C20:3	0.5±0.3	0.5±0.2	0.03±0.03	0.2±0.1
C20:4	3±0.5	5±0.2	4±1.0	4±0.5
Fatty acids (5 hr) (percent):				
C14:0	1±0.2	0.6±0.1	1±0.2	1±0.1
C16:0	39±3.0	47±3.0	46±5.0	43±3.0
C16:1	2±0.7	2±0.4	3±1.0	3±0.6
C18:0	8±1.0	6±1.0	6±1.0	6±1.0
C18:1	24±2.0	21±1.0	24±1.0	23±1.0
C18:2	23±3.0	18±1.0	16±3.0	21±1.0
C20:3	0.2±0.2	0.0±0.0	1±1.0	0.1±0.1
C20:4	3±0.0	5±1.0	4±1.0	3±0.5
L/O ratio (0 hr)	1±0.2	0.7±0.1	1±0.1	1±0.1
L/O ratio (5 hr)	1±0.1	0.9±0.1	1±0.1	1±0.1

¹ Noncardiovascular versus cardiovascular, not significant.

² SEM.

TABLE 6.—ESSENTIAL AMINO ACIDS REQUIRED BY MAN PER DAY AND IN WHOLE EGGS OR EGG YOLKS

Amino acid ¹	Required (d) ²	2 medium sized, shell-free, whole eggs (96 g) ³	2 medium sized egg yolks (34 g) ³
Isoleucine.....	0.70	0.81	0.37
Leucine.....	1.10	.99	.45
Lysine.....	.80	.80	.39
Methionine.....	1.10	.39	.13
Phenylalanine.....	1.10	.63	.25
Threonine.....	.50	.64	.33
Tryptophane.....	.25	.22	.10
Valine.....	.80	.96	.40

¹ Composition of amino acids in fresh whole eggs and fresh egg yolks, from: Everson, Gladys J. and Helen J. Souders. Composition and nutritive importance of eggs. J. Am. Dietet. Assoc., 33: 1244, 1957.

² W. C. Rose, R.L. Wixom, H. B. Lockhardt and G. F. Lambert. J. Biol. Chem. 217: 987, 1955.

³ Whole eggs, 11.7 g of protein and egg yolks, 5.4 g of protein, based on percent of protein in fresh whole eggs and fresh egg yolks: Nutritional Data. Harold A. Wooster, Jr. and Fred C. Blank, Heinz Nutritional Research Division, Pittsburgh, 1950, p. 86.

UNIVERSITY OF ILLINOIS,
Urbana-Champaign, Ill., May 31, 1977.

Senator GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs, U.S.
Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: Enclosed please find the write-up that you requested in your letter of May 2, 1977. I served on the subcommittee on dietary fats of the American Heart Association in 1968. Note that 150,000 copies of a diet heart statement contained a sentence which stated "Partial hydrogenation of polyunsaturated fats results in the formation of 'trans' forms which are less effective than 'cis, cis' forms in lowering cholesterol concentrations. It should be noted that many currently available shortenings and margarines are partially hydrogenated and may contain little polyunsaturated fat of the natural 'cis, cis' form." This statement was never distributed, because the Shortening Institute objected to it, and a new statement, that deleted the reference to "trans" fatty acids was printed and distributed. They are still present in our fats ten years after the Shortening Institute knew that they increased serum cholesterol levels. As far as I am aware, neither the American Heart Association or the NIH are funding a single research grant on the possible role of hydrogenated fats in heart disease. I had an NIH grant (HL 14273-06) on this subject, but it was not renewed.

You will note that I did a joint study with the FDA on the atherogenic activity of vitamin D. The FDA has worked quietly to remove vitamin D from highly fortified breakfast cereals. Isn't it strange that your diet recommendations do not mention vitamin D, hydrogenated fat nor the words of caution in the American Heart Association's Diet Heart Statement "Because cholesterol is abundant in many protein foods of high biological quality, careful planning is necessary to lower the intake of cholesterol without impairing the intake of foods high in protein." A tax on high calorie foods devoid of essential nutrients would decrease their consumption and lower fat intake without sacrificing good nutrition. It is unfortunate that the Congress has pressured

the NIH to spend millions of dollars on diet heart studies and the NIH is still doing so. Why not accept "the facts of life" and allow the researchers to uncover them? I hope you reopen the hearings and listen before advocating that Americans accept the recommendations on page 12 and 13.

Sincerely yours,

F. A. KUMMEROW,
Director, the Burnsides Research Laboratory.

AMERICAN HEART ASSOCIATION, INC.,
New York, N.Y., December 1, 1966.

FRED A. KUMMEROW, Ph. D.,
Professor of Food Chemistry, Burnsides Research Laboratory, University of Illinois, Urbana, Ill.

DEAR DOCTOR KUMMEROW: The American Heart Association is reviewing its most recent (June 1965) statement on Diet and Heart Disease, with a view toward possible revision, since scientific knowledge accumulates so rapidly in this field. The Association's Committee on Nutrition is establishing a small subcommittee for this purpose, under the chairmanship of Roslyn B. Alfin-Slater, Ph. D., Professor of Nutrition, School of Public Health, University of California, Los Angeles.

It is my pleasure to invite you to serve as a member of this group. Some of the work involved can be conducted by mail, but it is likely that several meetings will also be required before the proposed revision is submitted to the full Committee on Nutrition and other Association groups concerned. The Association provides reimbursement for travel and incidental expenses, according to the procedures described in the enclosed leaflet.

I would appreciate your early reply, through Dr. Nathaniel Cooper, of the American Heart Association staff, who will serve this subcommittee. I hope you will accept this important assignment.

Sincerely yours,

ROBERT E. HODGES, M.D.,
Chairman, Committee on Nutrition.

AMERICAN HEART ASSOCIATION, INC.,
New York, N.Y., July 9, 1968.

FRED A. KUMMEROW, Ph. D.,
Burnsides Laboratory, University of Illinois, Urbana, Ill.

DEAR FRED: Enclosed is another copy of the Diet and Heart Disease statement, together with the criticism of recommendation 2. offered by the Institute of Shortening and Edible Oils.

I have talked with Dr. Fred Mattson about this criticism and he believes it is entirely valid and that the statement, as printed, is inappropriate.

I must confess that I think our recommendations are not as accurate as they should be, particularly with regard to partial hydrogenation,

and the absolutely increased percentage content of polyunsaturates in the cis-cis form from 1961 to the present in shortenings, margarines and salad oils.

I have held up widespread distribution of the statement pending your recommendations on these criticisms.

Very truly yours,

CAMPBELL MOSES, M.D., *Medical Director.*

Enclosure.

DIET AND HEART DISEASE

(Revised Report of the Committee on Nutrition authorized by the Central Committee for Medical and Community Program of the American Heart Association—1968)

Atherosclerotic coronary heart disease results from many factors. Those which have been shown to be associated with this disease include:

1. Environmental factors such as customary diet, cigarette smoking and physical inactivity.
2. Inherited and acquired factors such as familial coronary heart disease, diabetes mellitus, hyperlipidemia, gout, hypertension, obesity and personality.
3. Sex and age; men are more susceptible than women, and both become increasingly susceptible with advancing years.

Some of these factors can be controlled, corrected or modified, Scientific studies are providing increasing evidence that diet is one important controllable factor.

The enormous burden of coronary heart disease and stroke as public health problems, and the growing probability that suitable measures will reduce the incidence of these diseases, led the American Heart Association to release two previous reports (in 1961 and 1965) on the relationship between diet and atherosclerosis. Since that time, additional scientific data have accumulated as a result of many different kinds of research activities. There is now strong evidence that appropriate dietary control may help to prevent or slow the progress of coronary heart disease. Accordingly, the American Heart Association, through its advisors, has revised its statement on diet and heart disease to include results of the latest scientific reports, [1, 2, 3]

Both epidemiologic studies of population groups and carefully controlled studies in animals have demonstrated that high concentrations of cholesterol in the serum are associated with atheromatous deposits in arteries. It has been repeatedly documented that in populations whose serum contains high concentrations of cholesterol, the incidence of atherosclerotic coronary heart diseases is high, whereas in populations with lower concentrations of cholesterol in their serum, the incidence of coronary disease is lower. It now is apparent that, if vascular lesions are to be prevented, prolonged elevation of serum cholesterol must be avoided. It seems equally apparent that lowering the concentration of cholesterol in the serum of human populations should be one of the first steps toward decreasing the incidence of coronary heart disease.

It has already been shown that in most (but not all) persons, the concentration of cholesterol in the serum can be decreased significantly

and can be maintained at a lower level by conscientious and sustained adherence to a nutritionally sound, modified fat diet. [4] It can be assumed that this type of diet will minimize the progressive rise in serum cholesterol concentration that generally occurs in most young adults. In general, a diet designed to decrease the risk of coronary heart disease involves the following recommendations:

1. *A caloric intake adjusted to achieve and maintain proper weight.*—Obesity is statistically associated with both hypertension and diabetes, and secondarily with coronary heart disease. Correction of obesity may also reduce serum lipid concentrations.

2. *A decrease in the intake of saturated and hydrogenated fats, and an increase in the intake of polyunsaturated fats.*—This will lower the concentration of cholesterol in the serum of most people. The exact quantity of fat needed in the diet is not known, but an intake of less than 40 percent of calories from fat is considered desirable. Of this total, polyunsaturated fats which are not hydrogenated should comprise twice the quantity of saturated fats. Many studies have shown that saturated fats elevate the serum cholesterol of man and that polyunsaturated fats lower serum cholesterol. The cholesterol-elevating effect of saturated fats is about twice as great as the cholesterol-lowering effect of polyunsaturated fats. Partial hydrogenation of polyunsaturated fats results in the formation of "trans" forms which are less effective than "cis, cis" forms in lowering cholesterol concentrations.* It should be noted that many currently available shortenings and margarines are partially hydrogenated and may contain little polyunsaturated fat of the natural "cis, cis" form.

3. *A substantial reduction of cholesterol in diet.*—The average diet in the United States contains about 600 mg. of cholesterol. This has been shown to have a significant effect on the concentration of cholesterol in the serum of most people. [5] Reduction of dietary cholesterol to less than half this amount is recommended. Because cholesterol is abundant in many protein foods of high biological quality, careful planning is necessary to lower the intake of cholesterol without impairing the intake of foods high in protein. For individuals with very high concentrations of serum cholesterol, even more marked restrictions may be necessary.

Other dietary factors: use of complex carbohydrates in preference to refined sugars. Dependence on foods such as vegetables, cereals and fruits to supply most of the dietary carbohydrates is preferable to excessive use of sugar, including candy, soft-drinks and other sweets. Replacement of complex carbohydrates by sugar may result in high concentrations of serum fats in susceptible individuals. [6] Epidemiologic studies have shown a relationship between excessive intake of sugar and diabetes and coronary heart disease. [7] Other dietary habits which have been shown to have some relationship to heart disease include the use of excessive amounts of coffee or alcohol. Available evidence fails to indicate that moderate use of coffee, alcohol or artificial sweeteners (cyclamates, saccharin) has a material effect on concentration of lipids in the serum or on the incidence of coronary heart disease in man.

*The terms "cis, cis" and "trans" refer to spatial arrangement of the carbon molecule of the fatty acid.

Any changes in the diet must preserve the principles of good nutrition. Although nutritional requirements differ during certain periods of the normal life cycle, the demands for optimal nutrition during periods of growth and development of infants, children, and adolescents, and of pregnant and lactating women, can be met by appropriate modification of the quantity of foods recommended under these dietary principles. [8] Life-long dietary habits which are formed during the developing years may influence the severity of atherosclerosis in later life.

Diets similar to those recommended herein have been consumed by many persons for periods of more than ten years without any evidence, clinical or biochemical, of deleterious effects. Furthermore, recent studies indicate that these diets effectively reduce both the concentration of cholesterol in the blood and the incidence of coronary heart attacks. [1, 2]

As already mentioned, coronary heart disease is a result of many factors. Dietary habits represent only one important risk factor that can safely be modified.

This statement is designed primarily for the scientific community. The American Heart Association has translated these dietary recommendations into several publications which are available to the general public and to patients through local Heart Associations and the AHA:

For patients, on a doctor's prescription only: "Planning Fat-Controlled Meals for 1,200-1,800 Calories" (EM 288); "Planning-Fat-Controlled Meals for Approximately 2,000-2,600 Calories" (EM 288A).

For the general public, no prescription required: Two companion booklets, "The Way to a Man's Heart" (EM 455) and "Recipes for Fat-Controlled, Low Cholesterol Meals" (EM 455A).

Although sodium restriction is not the subject of this statement, readers will also be interested in the following sodium-restricted diet publications, available to patients in two versions, each on a doctor's prescription only.

1. Booklet version: "Your 500 Milligram Sodium Diet" (EM 58); "Your 1,000 Milligram Sodium Diet" (EM 58A); and "Your Mild Sodium-Restricted Diet" (EM 58B).

2. Simplified leaflet version: "Sodium-Restricted Diet—500 Milligrams" (EM 380); "Sodium-Restricted Diet—1,000 Milligrams (EM 380A); and "Sodium-Restricted Diet—Mild Restriction (EM 380B).

All of the publications listed above are available to physicians, dietitians, and others in related professions.

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DIET AND HEART DISEASE

(This statement was developed by the Committee on Nutrition and authorized for release by the Central Committee for Medical and Community Program of the American Heart Association)

The development of atherosclerotic coronary artery disease is influenced by many factors; among the factors associated with an increase in this disease are:

1. A familial history of coronary heart disease; the presence of diabetes mellitus, hyperlipidemia, gout, hypertension, obesity, and certain personality characteristics.

2. Sex and age: Men are generally more susceptible than women and both become increasingly susceptible with advancing years.

3. Environmental factors such as a diet rich in saturated fat and cholesterol, cigarette smoking, and habitual physical inactivity.

There is growing evidence that the early identification and correction of these risk factors may favorably influence the course of coronary disease. For this reason, the American Heart Association has urged the implementation of risk factor identification programs (Risk Factors and Coronary Disease: a Statement for Physicians, A.H.A. 1968).

The fact that control of diet is one method of correcting or modifying some of these risk factors led the American Heart Association to release two previous reports (1961 and 1965) on the relationships between diet and atherosclerosis. Since that time, additional supporting data have been accumulated, particularly on the effects of diet on the occurrence rate of myocardial infarction. [1-5] Accordingly, the American Heart Association, through its advisors, has revised its statement on Diet and Heart Disease to include these reports.

It is most important to note that much of the data currently available on the relationship of diet to coronary artery disease are from studies using subjects unusually susceptible to coronary disease or atypical of the general population of the United States. There is an urgent need for more tightly designed, prospective studies involving larger numbers of healthy subjects so as to provide an unequivocal answer. A report on the feasibility of the dietary modifications for such a study has been published. [7]

It has been repeatedly documented that in populations with high concentrations of serum cholesterol, the frequency of atherosclerotic coronary heart disease is high, whereas in populations with lower concentrations of cholesterol in their serum, the frequency of coronary disease is lower. The evidence now indicates that avoidance of pro-

longed elevations of serum cholesterol can decrease the hazard of developing premature coronary disease.

It has already been shown that in most (but not all) persons, elevated concentrations of cholesterol in the serum *can be decreased* significantly and *can be maintained* at a lower level by conscientious and sustained adherence to a nutritionally sound, modified fat diet. [5, 7] It has been suggested, but it has not been proven, that this type of diet will minimize the progressive rise in serum cholesterol concentration that generally occurs in most adults.

DIETARY RECOMMENDATIONS

Although the dietary recommendations in this statement are designed for "healthy" individuals to reduce the risk factors influenced by diet, they are particularly applicable to individuals who are shown to have increased risk as determined by plasma lipid or lipoprotein concentrations. [7] In general, a diet designed to decrease the risk of coronary heart disease involves the following recommendations:

1. *A caloric intake adjusted to achieve and maintain proper weight.*—Obesity is statistically associated with both hypertension and diabetes, and secondarily, with coronary heart disease. Correction of obesity may also reduce elevated serum lipid concentrations.

2. *A decrease in the intake of saturated fats, and an increase in the intake of polyunsaturated fats.*—This will lower increased concentrations of cholesterol in the serum of most people. The ideal quantity of fat needed in the diet is not known, but an intake of less than 40 percent of calories from fat is considered desirable. Of this total, polyunsaturated fats should probably comprise twice the quantity of saturated fats. Many studies have shown that saturated fats elevate the serum cholesterol of man and that polyunsaturated fats lower serum cholesterol. The cholesterol-elevating effect of saturated fats is about twice as great as the cholesterol-lowering effect of polyunsaturated fats.

Considerable confusion has resulted from the regulation forbidding manufacturers to label vegetable oil products with their actual polyunsaturated fatty acid content. This has made it difficult to distinguish between a product "made with vegetable oil," but heavily hydrogenated (saturated) in manufacture, and one retaining a high content of polyunsaturates in the final product. Since 1961, many manufacturers have made a substantial effort to increase the polyunsaturate content of vegetable oil shortenings, the lightly-hydrogenated salad and cooking oils, and especially, the tub-type margarines. Accurate labeling would make it possible to identify the brands with a high-polyunsaturated fat content. For the present, margarines that are high in polyunsaturates usually can be identified by the listing of a "liquid oil" first among the ingredients. Margarines and shortenings that are heavily hydrogenated or contain coconut oil, which is quite saturated, are ineffective in lowering the serum cholesterol.

It should be noted that quite commonly, diets severely restricted in fats, with carbohydrate filling out the caloric requirement, may accentuate hypertriglyceridemia. Although the exact role of the triglycerides in atherogenesis is not clearly established, there is increasing evidence

that hypertriglyceridemia is associated with an increased incidence of coronary disease in younger men.

3. *A substantial reduction of cholesterol in diet.*—The average daily diet in the United States contains approximately 600 mg. of cholesterol. Sharp reduction in the amount of cholesterol in the diet has been found to lower the concentration of cholesterol in the serum of most people. [8, 10] In hypercholesterolemic individuals, reduction of dietary cholesterol to less than 300 mg. daily is recommended. Because cholesterol is abundant in many protein foods of high biological quality, careful planning is necessary to lower the intake of cholesterol without impairing the intake of foods high in protein.

Other dietary factors: Although there is a great deal of interest in the possible role of other dietary factors [9, 10, 11] (simple sugars vs. complex carbohydrates, alcohol, coffee and artificial sweeteners, such as the cyclamates and saccharin) in the development of coronary heart disease, the available evidence is incomplete. Dependence on foods such as vegetables, cereals and fruits to supply most of the dietary carbohydrates is preferable to excessive use of sugar including candy, soft drinks and other sweets.

In the application of these recommendations to family groups with a high incidence of coronary disease and/or with risk factors, any change in the diet must preserve the principles of good nutrition. Although nutritional requirements differ during certain periods of the normal life cycle, the demands for optimal nutrition during periods of growth and development of infants, children and adolescents, and of pregnant and lactating women can be met by appropriate modifications of the recommendations under these dietary principles.[10] Dietary habits which are formed during the developing years may continue life-long and influence the severity of atherosclerosis in later life. Diets similar to those recommended herein have been consumed by many persons for periods of more than ten years without any evidence, clinical or biochemical, of deleterious effects.

As already mentioned, coronary heart disease is a result of many factors. Diets rich in saturated fat and cholesterol represent one important risk factor that can be safely modified. Dietary management does not exclude appropriate use of drugs and other measures for control of risk factors.

This statement is designed primarily for the scientific community. A more detailed discussion of this subject is contained in "Modern Concepts of Cardiovascular Disease" for September-October, 1968.[7] The American Heart Association has translated these dietary recommendations into several publications which are available to the general public and to patients through local Heart Associations and the AHA:

For patients, on a doctor's prescription only: "Planning Fat-Controlled Meals for 1,200–1,800 Calories" (EM 288); and "Planning Fat-Controlled Meals for Approximately 2,000–2,600 Calories" (EM 288A).

For the general public, no prescription required: Two companion booklets, "The Way to a Man's Heart" (EM 455) and "Recipes for Fat-Controlled, Low Cholesterol Meals" (EM 455A).

All of the publications listed above are available to physicians, dietitians and others in related professions.

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STATEMENT BY PROF. FRED A. KUMMEROW, THE UNIVERSITY OF ILLINOIS

Mr. Chairman and members of the Senate Select Committee on Nutrition, I have been engaged in research on the chemistry and nutrition of dietary fats for 38 years on funds largely supplied by this Senate to the National Institutes of Health. These funds have made it possible for me, my students, and colleagues to publish more than 200 papers in journals devoted to the chemistry and nutrition of dietary fats and to support over 100 graduate students in their studies. Many of these students are presently employed in the food industry and some of them are directors of lipid research in the leading corporations of this industry.

I have read the report entitled "Dietary Goals for the United States" as prepared by the staff of the Select Committee on Nutrition and Human Needs, U.S. Senate, that was printed for this committee and dated February, 1977. On pages 12 and 13, these goals were summarized as follows:

- (1) Increase carbohydrate consumption to account for 55 to 60 percent of the energy (caloric) intake. (2) Reduce overall fat consumption from approximately 40 to 30 percent of energy intake. (3) Reduce saturated fat consumption to account for about 10 percent of total energy intake; and balance that with polyunsaturated and mono-unsaturated fats, which should account for about 10 percent of energy intake each. (4) Reduce cholesterol consumption to about 300 mg. a day. (5) Reduce sugar consumption by about 40 percent to account for about 15 percent of total energy intake. (6) Reduce salt consumption by about

50 to 85 percent to approximately 3 grams a day. The goals suggest: (1) Increase consumption of fruits and vegetables and whole grains. (2) Decrease consumption of meat and increase consumption of poultry and fish. (3) Decrease consumption of foods high in fat and partially substitute poly-unsaturated fat for saturated fat. (4) Substitute non-fat milk for whole milk. (5) Decrease consumption of butterfat, eggs and other high cholesterol sources. (6) Decrease consumption of sugar and foods high in sugar content. (7) Decrease consumption of salt and foods high in salt content.

These dietary goals and suggested changes in proper food selection would provide for better nutrition to someone informed in food composition and food processing. However, most people would simply drop out of their diet the eggs and "other high cholesterol sources" that are listed as foods to decrease and substitute food items that please their palate, but provide only calories to satisfy the hunger pangs that stimulates food intake. These dietary recommendations do not take into consideration that "high cholesterol sources" supply essential protein and that the large advertising budget of \$1,159,522,600/yr. is a prime motivator for change in food consumption patterns. The ad copy writers take their cue from the recommendations encompassed in the dietary goal patterns and "fill" into their copy as "substitutes for other high cholesterol sources" the particular food item that they are trying to sell [1, 2].

The consumer "gets the message" by urgings, for example, to change from whole eggs to substitute eggs and from breakfast sausage and bacon to substitute products made from soybean meal. The providers of these substitutes have not tested, in animal models or human subjects, their nutritional value, their ability to lower serum cholesterol or their possible influence on atherosclerosis. The responsibility to do so is deemed unnecessary because their processors have been urged to provide such items and, therefore, feel no responsibility for testing them. Since they are simply supplying a substitute food item at the suggestions of the highest medical authorities in the country, the nutritional testing of such substitutes for efficacy does not seem necessary to them. This is a unique type of thinking that is not applied by the EDA to other food items in the American diet. The ingredients in the substitutes are acceptable food sources, however, they are not equal to the nutritional value of the food items they were prepared to replace. The introduction of such substitute food items, which are non-toxic in character, but do not have the nutritional value of the food they are intended to replace, provides a new parameter of jurisdiction for the Food and Drug Administration (FDA).

These dietary goals can be taken one at a time and their total impact on the American diet considered. For example, it would be desirable to increase the consumption of bread, made from higher extraction flours, which contain more fiber and protein. However, these flours also contain more insect fragments and under present FDA regulations are impossible to market [3]. Furthermore, the assumption that decreasing fat consumption and increasing carbohydrate consumption will lower serum cholesterol levels on the basis of ad libitum consumption has not been adequately tested. For example, villagers in the Transylvania region of Romania that consume a diet which contained 38 percent fat did not have any higher serum cholesterol levels than villagers that consumed 28 percent fat or 188 and 187 mg percent, respectively (Table 1).

One must also take two other factors into consideration. One, that the satiety value of fat decreases food consumption in an *ad libitum* diet situation and two, that most natural fats contain linoleic acid and, therefore, contribute to the total PUFA intake. Excess carbohydrate consumption in a surfeit diet will result in an increased *in vivo* synthesis of fat and its deposition in the tissue. The most obvious means of lower serum lipid levels is not mentioned in these diet recommendations, that is, to cut down on total caloric consumption [4].

The consumer has no control over fat composition; on the other hand, the processor does. Approximately 6.8 billion pounds of soybean oil/year is hydrogenated which converts a liquid oil high in PUFA into a saturated fat in order to stabilize the oil against oxidation. A liquid high PUFA oil, such as corn or cottonseed oil, is blended with this hydrogenated fat in proportion that depends on the processor's formulation rather than on nutritional need. Thus, some margarines contain three times more PUFA than others and shortenings also vary in formulation. For the consumer to reduce saturated fat intake by 10 percent and to increase unsaturated fat intake by 10 percent would require more knowledge and a control over processing of fats that is not available to the consumer or the government. The processor is also limited because corn and cottonseed oil is a by-product [5] of industrial processes and their availability is limited by price and production (Table 2).

Table 9 on page 44 is instructive to one interested in the sugar intake. Household consumption of sugar has actually decreased from 52.1 pounds in 1909 to 24.7 pounds in 1971 and further decreases in household use is unlikely. The greatest increase in sugar consumption was due to soft drinks from 3.5 pounds in 1909 to 22.8 pounds in 1971. It has doubled from 1949 to 1971 and has increased since. How can the consumer make a connection between decreasing sugar consumption and diet recommendations when household sugar consumption is only $\frac{1}{2}$ of what it was in 1909, and not a word is said about soft drinks as the main source of sugar in teenage diets? The Congress should tax soft drinks rather than lobby against them and use the tax as a subsidy for fruit and vegetable production.

To reduce salt consumption could mean using the salt shaker at the table less often, however, the major source of salt is provided by potato chips, salted peanuts, pizzas, and preservatives. In Japan and rural Romania, salt is used to preserve vegetables; the total salt intake is higher than in the United States and so is the rate of cerebral atherosclerosis [6]. Americans will continue to eat potato chips and pizzas in quantity until a tax is also levied against these food items. Potato chips taste delicious to most people and telling them to decrease their consumption will not make much of an impression on them.

The greatest error in the dietary goals rests in calling attention by name to the very food items that have been eaten in quantity by countless generations and are still stable food items in rural population groups in which the rate of coronary heart disease is 10–20 times lower than in the urban areas in these countries or the United States. Men living in the remote mountain areas of Transylvania eat more than two eggs/capita/day and rarely suffer from coronary heart disease. Population groups in urban areas of Romania that eat less meat than Ameri-

cans want to eat more meat than is available to them. Furthermore, slaughter practices differ in the United States and Europe. In the United States, most of the lungs, spleen, stomach, and entrails are converted to dried meat scrap and used in dog and cat food. In Europe, these products are made into sausage and almost as much sausage as meat is consumed/capita [7].

The diet goals assume that the butterfat in whole milk or the egg yolk in eggs is not used as human food. In actual practice, much of the excess butterfat is used in ice cream and egg yolk is used in the manufacture of mayonnaise, macaroni and noodles [8]. To recommend skim milk instead of whole milk and eggs devoid of egg yolk represents neither good nutritional or economic sense.

Population groups that eat less "visible" fats and sugar do have a lower serum lipid level and less coronary heart disease than Americans. However, they are more physically active than Americans, and their diets do not contain hydrogenated vegetable fat, shortening, margarine, soft drinks, potato chips, french fries, cream pies, doughnuts, and pizza. The consumption of these sources of unnecessary calories should be drastically reduced in the American diet and that will require a media exposure worth one billion dollars because these items are heavily advertised. One hundred million dollars worth of "nutrition education" can't hope to match their impact on the American diet. The cholesterol-containing foods, such as meat, eggs, cheese, and milk, provide the major share of protein, calcium, and other essential nutrients to the American diet. A drastic decrease in their intake by children would cause profound changes in growth patterns and stunting of growth. Is anyone willing to take such risks? What proof is there that the rate of heart disease will decrease?

Americans have consumed 600 mg of cholesterol/day/capita since 1909 (Table 3). Reducing red meat intake and increasing chicken and fish intake will not reduce cholesterol intake as chicken and fish also contain cholesterol [9]. Reducing the cholesterol intake to 300 mg/day may only result in further increase in fat intake as food consumption is based on caloric need rather than percentage composition. The importance of total caloric intake to the rate at which atherosclerosis developed in a nonhuman primate has been documented by Wissler, et al.

Rhesus monkeys fed a prudent diet, which coincides with the diet recommendations by the National Research Council of the National Academy of Sciences for this animal model [10], resulted in less atherosclerosis than a diet higher in calories or 16 and 30 g/day of fat, respectively (Table 4). However, the arteries of some of the monkeys on the prudent diet were also atherosclerotic. To minimize the development of this disease process, it seems prudent to consume an adequate amount of foods high in protein, vitamins, and minerals, such as meat, eggs, and milk, and a sufficient amount of fruits and vegetables and carbohydrate-containing foods, such as bread, cereals, and economical sources of fat, for enough calories to maintain weight. As the metabolic defect that causes thickening of the arterial wall remains unknown, it would seem most judicious to consume a diet composed of food items which have been used for countless generations and not to drop them out of the diet because they happen to contain "invisible" animal fat or cholesterol.

The intake of "visible" animal fats, such as butter and lard, had decreased from 21.9 in 1950 to 10.2 pounds/capita in 1975 and the intake of vegetable fat has increased 24.0 to 43.1 pounds during the same time period [9]. Approximately two-thirds of these 43 pounds of vegetable fats are hydrogenated or converted to a "saturated" fat in order to stabilize it against oxidation. Population groups which do not consume such hydrogenated fats do not suffer as much heart disease as those that do. Animal models fed such fats deposit more fat in their hearts than those fed natural unhydrogenated fats [11]; the heart mitochondria oxidizes them at a slower rate than natural fats [12] and they influence the lipid composition and properties of cell membranes [13-18] and possibly the development of atherosclerosis. [1]. Other risk factors, such as vitamin D, should not be considered [19].

The Senate Select Committee has focused on a problem which good nutrition may help to minimize. I suggest that the present barrage on TV that is leveled at children and their mothers be countered with informative ads similar to the technique that was used on TV cigarette ads. If the Senate is vitally interested in solving the problem of heart disease, it should provide increased funding of the National Heart and Lung Institute for research grants to solve this problem as only 27 percent of approved grants in the area of nutrition are presently funded. No one at present knows what causes "heart disease." I personally believe that less pressure should be applied to the NIH for quick solutions and more funds should be allocated to basic research in nutrition. Heart disease is due to a complex biochemical process which, in time, will be identified; that time schedule depends more on the Congress than researchers.

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TABLE 1.—RESULTS OF SURVEY IN SEVEN VILLAGES IN TRANSYLVANIA, ROMANIA, IN 1962

Village	Number persons	Calories per day	Percent lipid in diet	Serum cholesterol (milligrams percent)	Total serum lipid
Marisel.....	412	2,895	20.0	137	721
Avram Iamu.....	94	2,990	23.0	140	804
Finigal.....	130	3,023	25.0	157	-----
Corna.....	87	3,623	28.0	187	850
Sintana.....	171	3,883	34.0	176	761
Vlaka.....	130	4,137	38.0	188	-----
Culenesti Oas.....	102	3,051	20.7	135	709

Note. Margarine introduced in 1968; present consumption in urban areas equals 2-3 kilo/year/capita. These villages are presently being resurveyed. The results to date indicate an increase of 40 milligrams percent in serum cholesterol values.

TABLE 2.—FATTY ACID COMPOSITION OF MARGARINE METHYL ESTERS
[Weight percent]

Fatty acid ¹	Margarine											
	A	B	C	D	E	F	G	H	I	J	K	L
12:0	0.04						0.08	0.10	0.17	0.04		0.04
14:0	11.38			0.05	0.08	0.11	0.27	0.28	0.14	0.09		0.04
16:0	11.38			10.94	11.34	11.51	16.92	16.62	11.86	10.82	11.50	11.29
16:1 <i>n</i> -7				7.18	6.18	7.20	5.11	5.21	6.19	6.19	6.24	6.22
18:0	7.05	4.79	6.59	7.38	6.91	7.55	5.33	5.06	6.78	6.65	6.72	6.49
18:1 <i>n</i> -9 c	35.22	30.38	29.30	26.20	27.02	35.47	28.53	26.56	27.82	32.04	25.24	23.75
18:1 <i>n</i> -9 t	31.41	6.88	14.26	21.70	13.19	30.77	15.29	13.70	20.07	15.57	22.03	11.36
18:2 <i>n</i> -6 c	9.78	39.69	33.01	28.84	34.67	9.37	23.25	24.82	30.33	28.83	32.08	43.98
18:2 <i>n</i> -6 t, <i>cl</i>	4.07	2.49	2.49	1.05	1.80	3.75	6.95	8.59	1.68	3.41	1.24	0.73
18:3 <i>n</i> -3	.50	2.87	2.75	3.78	4.13	.66	2.02	2.22	.54	1.89	.60	.83
Others	.32	.66		.28	.68	.61	1.25	1.84	.42	.47	.29	.30
Total trans GLC ¹	35.48	9.87	16.75	22.75	14.99	34.50	22.24	22.29	21.75	18.98	23.56	12.41
Total trans IR-1 ²	35.00	15.50	31.50	26.75	20.50	37.75	30.75	26.50	27.70	25.50	28.50	16.50
Total trans IR-2 ²	35.50	14.25	30.80	25.00	16.50	33.00	22.50	24.25	21.50	23.50	30.00	16.00

¹ Gas chromatography was accomplished with a 20 ft. \times $\frac{1}{8}$ in. S.S. column packed with 15 per cent OV-275 coated on 100-210 mesh Chromosorb P (AW-DMCS) at 220C. Injector, 240C, detector, 300C; instrument, HP Model 5830; carrier gas flow, 10 ml N₂/m n.

² IR analysis carried out in 2 different laboratories on 2 different instruments.

TABLE 3.—ANNUAL PER CAPITA CONSUMPTION OF ANIMAL FOOD PRODUCTS

Year	Meat		Poultry		Fish		Eggs		Dairy products		Animal fat		Total pounds linoleic acid	Total cholesterol ²
	Pounds	Pounds of linoleic acid ¹	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid	Pounds	Pounds of linoleic acid		
1909	146.6	0.70	15.9	0.38	13.9	0.47	35.1	0.63	178	0.18	12.4	0.43	2.8	545
1960	146.9	.71	34.6	.83	13.2	.45	42.5	.76	238	.24	7.5	.26	3.3	614
1961	145.9	.70	37.8	.90	13.7	.47	41.7	.75	235	.24	7.4	.26	3.3	563
1962	147.1	.71	37.4	.90	13.6	.46	41.4	.75	235	.24	7.3	.26	3.3	609
1963	152.0	.73	37.9	.91	13.7	.47	40.4	.73	234	.23	6.9	.24	3.3	610
1964	155.7	.75	38.9	.93	13.5	.46	40.4	.73	235	.24	6.9	.24	3.4	616
1965	148.3	.71	41.3	.99	13.8	.47	39.7	.72	234	.23	6.4	.22	3.3	602
1966	151.4	.73	44.3	1.1	13.9	.47	39.7	.71	234	.23	5.7	.20	3.4	607
1967	158.3	.76	46.2	1.1	13.6	.46	40.6	.73	230	.23	5.5	.20	3.5	623
1968	162.4	.78	45.8	1.1	14.0	.48	40.1	.73	231	.23	5.7	.20	3.5	628
1969	161.4	.77	47.8	1.1	14.2	.48	39.3	.71	230	.23	5.4	.19	3.5	633
1970	164.6	.79	50.1	1.2	14.8	.50	39.5	.71	226	.23	5.3	.19	3.6	628
1971	170.0	.82	50.3	1.2	14.4	.49	39.9	.72	228	.23	5.1	.18	3.6	639
1972	166.5	.80	52.5	1.3	15.3	.52	39.0	.70	228	.23	4.9	.17	3.7	631
1973	154.6	.74	50.5	1.2	15.6	.53	37.2	.67	229	.23	4.8	.17	3.5	600

¹ Calculations of pounds of linoleic acid based upon assumption that amount of linoleic acid in certain foods has not changed over the past 60 years. (Fat Content and Composition of Animal Products, the National Research Council, December 1974.)

² Milligrams per day as calculated from the total per capita intake of each food item and its cholesterol content. (J. Am. Oil Chemists' Soc. 27: 414, 1950.)

TABLE 4.—COMPOSITION OF THE TABLE PREPARED HUMAN DIETS FED TO RHESUS MONKEYS

Item	Nutrient			American diet					Prudent diet					
	Percent protein	Percent fat	Percent C18:2	Choles-terol mg/100g	Amount (gm)	Protein (gm)	Fat (gm)	C18:2 (gm)	Choles-terol (gm)	Amount (gm)	Protein (gm)	Fat (gm)	C18:2 (gm)	Choles-terol (gm)
Dry milk	35.6	1.0	3	---	11	3.92	0.11	---	---	10	3.56	.10	---	---
Eggs	12.8	11.5	19	468	10	1.28	1.15	.30	46.8	0	0	---	---	0
Beefs	17.4	23.0	2	95	15	2.61	3.45	.07	15.8	5	.87	1.15	.02	5.3
Beef fat	0	100	2	75	2.4	0	2.40	.05	3.2	0	0	---	---	0
Pork	16.4	25	9	60	7.0	1.15	1.75	.63	11.7	3.0	.49	.75	.27	5.0
Pork fat	0	100	9	108	1.6	0	1.60	.14	1.48	0	0	---	---	0
Salmon	21.4	7.0	20	60	3.0	.64	.21	.04	5.0	6.0	1.28	.42	.08	10.0
Chicken	20.2	12.6	22	90	6.0	1.21	.76	.16	6.7	18.0	3.64	2.27	.48	20.0
Turkey	20.1	20.2	22	90	0	0	---	---	0	8.0	1.61	1.62	.36	8.9
Liver	19.8	4.2	38	320	2	.40	.08	.30	.62	0	0	---	---	0
Cheese	23.9	32.3	3	160	2.4	.57	.77	.02	1.5	0	0	---	---	0
Cottage cheese	19.8	.8	3	---	0	0	---	---	---	3.0	.59	.02	0	0
Bread	8.5	2.0	9	---	36.0	3.06	.72	.06	---	36.0	3.06	.72	.06	---
Potato	2.0	1	24	---	20.0	.40	.02	---	---	20.0	.40	.02	---	---
Carrots	7	2	18	---	20.0	.14	.04	4.8	---	20.0	.14	.04	4.8	---
Lettuce	1.2	2	52	---	10.0	.12	.02	1.8	---	10.0	.12	.02	1.8	---
Cereal	7.9	7	---	---	4.0	.32	.03	2.08	---	0	0	---	---	0
Banana	1.2	2	---	---	20.0	.24	.04	---	---	20.0	.24	.04	---	---
Apple	.3	4	---	---	20.0	.06	.08	---	---	20.0	.06	.08	---	---
Pound cake	6.4	8.2	3	20	8.0	.51	.66	.24	4.0	0	0	0	0	0
Orange juice	.9	.2	---	---	24.0	.21	.04	---	---	24.0	.21	.04	0	0
Sugar	0	0	---	---	18.0	0	0	0	0	9	0	0	0	0
Cottonseed oil	0	100	45	0	1.8	0	1.80	.81	0	0	0	0	---	0
Saturated margarine	.6	80	9	0	4.4	.02	3.52	.40	0	0	0	---	---	0
PUF margarine	0	80	32	0	0	0	---	---	---	3.0	.02	2.4	.96	0
Corn oil	0	100	50	0	0	0	---	---	0	7.0	0	7.0	3.50	0
Butter	.6	81	3	185	9	.05	.729	.22	4.86	0	0	---	---	0
Lard	0	100	9	120	2	0	2.0	.18	1.67	0	0	---	---	0
Bacon	9	65	9	50	3	.03	1.95	.17	6.0	0	0	---	---	0
Total	---	---	---	---	---	16.94	28.56	3.56	109.33	---	16.29	11.21	5.73	49.2

Source. Wissler, R. The Myocardium: Failure and Infraction. E. Braunwald, ed. PH Publishing Co., N.Y. 1974.

BAYLOR COLLEGE OF MEDICINE,
TEXAS MEDICAL CENTER,
Houston, Tex., May 20, 1977.

Senator GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs,
Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you very much for writing to me and for the copy of the Dietary Goals for the United States. One of my colleagues, Doctor Antonio M. Gotto, Jr., who serves with me as Scientific Director of the Cardiovascular Center and is Chairman of the Department of Medicine at Baylor, testified before your Committee on February 1, 1977. I am in agreement with Doctor Gotto's statement and would like to underline and emphasize the importance of public education in achieving your objectives.

Doctor Gotto, in his testimony, referred to some of the public education activities being supported through the National Heart and Blood Vessel Research and Demonstration Center here at Baylor College of Medicine. We are attempting to develop models which could be applied to the entire country. We believe that the major focus must be on education of the public. In my opinion, in our society the way to change national habits in a desirable way is through public education and not through mandatory laws.

In his testimony, Doctor Gotto recommended the organization of a state of the art workshop in nutrition in an attempt to reach an agreement between various groups concerning dietary recommendations for the American public. This would seem to be a worthwhile objective. Doctor Gotto and I agree with your goals of reducing consumption of fat, saturated fat and cholesterol. We do not believe that there is scientific documentation for the recommendations on limiting the intake of sugar and salt, although these measures are of obvious importance in selected patients such as diabetics, hypertensives or those with congestive heart failure. We believe it would be a mistake, however, for the recommendations to go beyond the scientific evidence available in these areas.

We were concerned that your report did not give much attention to diabetes mellitus, which has become a major health problem related closely to cardiovascular disease and diet. Other areas where additional attention might be given are those of vitamin and mineral consumption, nutrition in children and total caloric intake.

We participated in Doctor Norum's survey to which you made reference in your letter, but would caution you that this could hardly be considered a scientific document or scientific survey.

In summary, my overall impression of the objectives of your Committee are favorable. The major emphasis should be on education. I am opposed in general to mandatory laws regulating the diet and caution against recommendations which go beyond what is documented by scientific evidence.

I appreciate the opportunity to respond to your proposal and to the predigious and excellent work by yourself, your Committee and your staff.

Yours sincerely,

MICHAEL E. DEBAKEY, M.D.

THE WISTAR INSTITUTE,
Philadelphia, Pa., May 24, 1977.

Senator GEORGE MCGOVERN,

Chairman, U.S. Senate Select Committee on Nutrition and Human Needs, Washington, D.C.

DEAR SIR: Thank you for sending me a copy of "Dietary Goals for the United States" and for the gratifying request to comment on this publication.

I believe there is much in this report which will be educational for the American public and of which your committee can be proud. My reservations are based on the fact that although you clearly recognize the controversial nature of the data (page 10), this caveat is never again stated and the general impression is given that adherence to the prescribed goals will be a sure way of avoiding a number of disease states. Because of their imprecise nature, epidemiological data may be useful for making predictions for populations but not for individuals. There are data which indicate that elevated cholesterol levels are correlated with the risk of coronary disease, but there are none which show that lowering cholesterol levels decreases risk; that is an assumption. Risk factors are statistical rather than medical diagnoses. Lande and Sperry (*Archives of Pathology* 22: 301, 1936) showed that cholesterol levels in men aged 11-80 who came to autopsy were all in the same range and did not correlate with the cholesterol content of their aortas, which rose with increasing age.

There is an increasing awareness that coronary disease is a "life-style" disease and diet is only one aspect of life style, albeit one which can be easily amended. I was a participant in the Norum survey which you quote in your letter of April 29. I felt that the questions on diet would have provided a better reflection of the respondents views if we had been asked to rate the importance of fat, carbohydrate, etc. on a 1-5 scale rather than answer yes or no. Almost everyone thinks diet had some connection with heart disease, but the major argument concerns the extent of that connection. When Norum asked what would be the first change his panel would recommend for the public or themselves it was reduction in total calories.

This reply bears on obesity, a condition which may be the most widespread nutritional disease in the United States. The Committee report says relatively little about the medically disagreeable concomitants of obesity or about alcohol as an important source of calories.

Enclosed is a reprint (*American Journal of Pathology* 84: 615, 1976) of a paper which was presented in a Symposium on "The Role of Nutrition in the Pathogenesis of Disease" held at the sixtieth annual meeting of the Federation of American Societies of Experimental Biology in Anaheim, California, April 12, 1976. In this review I tried to develop the theme that everything in the diet could affect serum cholesterol levels—lipid, protein, carbohydrate, fiber, and trace minerals. How each affects blood cholesterol and atherosclerosis and how these components interact to counteract or reinforce each other has to be worked out.

There is potential danger in suggesting sweeping remedies when evidence is still circumstantial. Let me cite one example. A few years ago dietary fiber (an area of nutrition which for many years had been investigated without publicity) was suddenly brought to the attention of the public and the particular type of fiber which was said to

cure all ills was bran. Use of bran as a cholesterol lowering agent was widely recommended in the professional and lay press. In 1975 it might have seemed that bran should be added to all diets by fiat. The results of ten publications on the effects of bran on serum lipids in man were collated by Truswell and Kay (*Lancet* 1:367, 1976). In a rare show of unanimity nine of the ten studies found no effect on serum cholesterol levels; the tenth detected a modest (7 percent) reduction.

Connor and Connor (*Preventive Medicine* 1:49, 1972) presented data tending to correlate cholesterol intake with the incidence of coronary disease in men aged 55-59 years. The United States showed the highest cholesterol intake and highest death rate. Finland had the second highest death rate on a cholesterol intake half of our. France had a cholesterol intake slightly higher than Finland's but a death rate that was 79 percent lower.

Two other findings that are germane to the cholesterol question have recently appeared. One is a rediscovery of an observation by Barr, Russ and Eder (*American Journal of Medicine* 11:480, 1951) that the lipoprotein fraction in which serum cholesterol is transported is more meaningful than the total cholesterol vis-a-vis coronary disease. The new papers on this point (Castelli et al., *Circulation* 55:767, 1977; Miller and Miller, *Lancet* 1:16, 1975; Rhoads, Gulbrandsen and Kagan, *New England Journal of Medicine* 294:293, 1976) suggest that the ratio of high to low density lipoprotein cholesterol may be the real factor determining susceptibility. What profiteth a man to lower HDL cholesterol? The other finding, by Imai et al. (*Archives of Pathology and Laboratory Medicine* 100:565, 1976), suggests that "old" cholesterol contains oxidation products which are the major source of damage to the aorta and coronary vessels. These oxidation products arise in cholesterol which is stored. The extension of this observation (if borne out) is that those food products which are made with dried, stored ingredients containing cholesterol may be more injurious than those containing "fresh" cholesterol.

Finally, I would like to cite a recent report by Nichols et al (*Journal of the American Medical Association* 236:1948, 1976) who studied serum lipids and diet in 4057 participants of the epidemiological cardiovascular study carried out in Tecumseh, Michigan. They found no positive correlation between cholesterol or triglyceride levels with fat, sugar, starch, alcohol, coffee or tea.

In relating diet to cancer (page 33) your report suggests a high correlation between meat consumption and colon cancer. Let me apprise you of the recent report by Lyon et al. (*New England Journal of Medicine* 294:129, 1976) who found that Mormons (who eat as much meat as most Americans) have rates of colon cancer 35 percent below the standard incidence rate. Animal experiments (Carroll, *Cancer Research* 35:3374, 1975) further indicate that rats fed a chemical carcinogen plus 20 percent unsaturated fat exhibit a much greater incidence of tumors than when fed saturated fat. The average incidence of tumors per 30 rats in animals fed any of five unsaturated fats was 117 whereas for rats fed four saturated fats it was only 82. Reddy et al. (*Cancer Research* 35:3421, 1975) also found that rats treated with a carcinogen and fed 5 percent corn oil exhibited 3.5 times the incidence of colon tumors than did treated rats who were maintained on 5 percent lard. A similar relationship was observed in tumors at other sites.

I agreed with the 1969 report of the Diet-Heart Review Panel (American Heart Association Monograph 28, 1969) that the time was not ripe for recommending wholesale dietary changes. I don't think the situation has changed.

I believe that your Committee Report can be a useful document for providing Americans with information on dietary effects. I think that one general goal should have reduced caloric intake so that optimum weight was achieved. As the diet recommended by your committee now stands (page 12), it would achieve only a 10 percent reduction in calories. I feel that there should be no promise that suggested changes can affect the course of disease. I also think that, since your own staff recognized the controversial nature of the data, contrary opinions should have been included so that the reader could see both sides of the question.

I am bothered that some comments have made it appear as if there is an adversary relationship among people discussing this report. Everybody in the field of nutrition is motivated towards the same goal, namely, to discover the basic relationship between diet and disease and thus lay the groundwork for dietary recommendations. The differences lie only in the perception of how far the data can take us.

I agree that the public should be better educated in health and nutrition but that this education should be general and not narrowed down to the dietary goals expressed on page 13. I also feel that a strong effort should be made to include nutrition education in all medical school curricula. For the present I feel the best dietary advice is: Moderation, not martyrdom.

I should again like to express my admiration for the work and mission of your committee and my gratitude for being asked to offer an opinion.

Sincerely yours,

DAVID KRITCHEVSKY, Ph. D.,
Associate Director.

Enclosure.

DIET AND ATHEROSCLEROSIS

(By David Kritchevsky, M.D.*)

Because of the statistical establishment of elevated blood lipids as a risk factor in the development of atherosclerotic heart diseases, most of the attempts to regulate blood lipids by diet or centered on the fat in the diet. The levels of blood lipids and the course of experimental atherosclerosis can be effected by other dietary components such as type and amount of protein, carbohydrate, and nonnutritive fiber. Interaction among the dietary components further affects serum lipids and atherosclerosis. (Am J Pathol 84:615-632, 1976)

Long-term studies [1, 2] have clearly shown that elevated serum cholesterol levels are one of the principal indications of a susceptibility to atherosclerotic coronary heart disease (ASHD). Hurxthal [3] and

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Page [4] and their co-workers have demonstrated that blood cholesterol levels may have a predictive value in individuals. In addition to serum cholesterol levels, serum triglyceride levels have been shown to be correlated with incidence of ASHD, [5, 6] as have the serum lipoprotein levels. [7, 8] However, as Shanoff [9] has pointed out, many of the factors that are highly correlated with the etiology of ASHD in a given population may not tell much for any individual.

The implication of the serum lipids in the development of ASHD has made them the focus of attempts to moderate the course of this disease or to prevent it. The thrust of most of the dietary studies has been to evaluate the premise that high levels of serum lipids are due primarily to increased intake of dietary fat and that reduction or alteration of the lipid in the diet will lower the levels of lipids in the blood and, hence, reduce the risk and incidence of ASHD.

The purpose of this exposition is not to expand on the lipid hypothesis, which is well established, but rather to show that the serum lipids (and the course of ASHD) can be affected by dietary components other than lipid. It is essential that the total diet be examined, as there are few susceptible populations subjected to the monotony of a single-component diet.

The one aspect of the American diet which has borne the brunt of the attack has been lipid. The general thesis has been that since the beginning of this century the amount and type of fat in our diet has changed and that this change underlies the increase in coronary heart disease. However, everything in the diet has changed. Friend [10] has summarized the changes in the availability of nutrients in the United States since 1909. Some of her data and those of Gortner [11] and Rizek *et al.* [12] are summarized in Table 1. It is evident that several important changes have occurred in the American diet since 1909. While protein availability has not changed much, the ratio of animal to vegetable protein has doubled. Carbohydrate availability has fallen by 21 percent, and the level of dietary fiber has fallen by 30 percent since 1909 [11] and by 47 percent since 1880. [13] Fat availability has increased by 26 percent since 1909; the intake of animal fat has fallen by 7 percent and that of vegetable fat has increased by 181 percent. The ratio of polyunsaturated to saturated fatty acids was 0.21 in 1909 and 0.43 in 1974. Cholesterol availability was 509 mg in 1909 to 1913 and 556 mg in 1970. The peak intake was 578 mg in 1957 to 1959 and the average (1909 to 1970) was 540 mg. In the period 1900 to 1960, the death rate from heart disease rose from 130/100,000 to 355/100,000.

Masironi [14] compared diet and cardiovascular death rates in a number of countries between 1955 and 1965 and found no clear trends. Thus, in the United States there was a 4 percent increase in death rate and a decrease in saturated fat intake and in total calories. In Switzerland, with a 5.5 percent increase in death rate, the total intake rose by 28 percent and the saturated fat intake by 18 percent. Finland, which showed a 30 percent increase in death rate, exhibited a 34 percent increase in saturated fat intake and a 123 percent increase in sucrose consumption. In Yugoslavia, the death rate increased three- to fourfold, the saturated fat intake fell by 26 percent but that of sucrose almost tripled. The data suggest that many factors in the diet play a role in ASHD; this exposition proposes to touch on each dietary class.

TABLE 1.—TRENDS IN PER CAPITA NUTRIENT AVAILABILITY¹

	Calories	Protein		Carbo- hydrate (g)	Fat		Fatty acids (g)		
		Total (g)	A/V		Total (g)	A/V	Sat	18:1	18:2
Year:									
1909-13-----	3,490	102	1.06	492	125	4.88	50.3	51.5	10.7
1925-29-----	3,466	94	1.20	476	135	2.69	53.3	55.2	12.5
1935-39-----	3,270	90	1.27	430	135	2.85	52.9	54.5	12.7
1947-49-----	3,230	95	1.78	403	141	2.88	54.4	58.0	14.8
1957-59-----	3,140	95	2.06	374	143	2.41	54.7	58.2	16.6
1965-----	3,160	96	2.19	371	145	1.94	53.9	58.8	19.1
1972-----	3,320	101	2.37	381	158	1.64	55.9	63.1	23.3
1974-----	3,350	101	2.26	388	158	NA	56.0	62.9	24.2

¹ After Friend, Gortner, and Rizek et al.

Note: A/V, animal origin/vegetable origin; NA, not available, Sat, saturated.

LIPID

The occurrence of cholesterol in animal fat and the lower iodine value of fat of animal origin, together with various epidemiologic data, suggest that cholesterol-lowering diets should be rich in polyunsaturated fats. A number of primary prevention studies [15-17] have reported lowered serum cholesterol levels in men fed diets high in unsaturated fat. The number of myocardial infarctions were also lower in the test group. A secondary prevention trial in Oslo [18] showed that men placed on a diet high in unsaturated fat had fewer myocardial infarctions, but a similar trial in England [19] was without effect. Could the rest of the diet have played a role?

In animals there is ample evidence that diets containing cholesterol and saturated fat are more atherogenic than similar diets in which the fat is unsaturated. [20, 21] Saturated fats can even be atherogenic in semi-purified diets containing no cholesterol, [22-24] but as we shall see below, the observed effect is not due to the dietary fat alone.

However, unsaturation of a fat is not a guarantee of a beneficial effect. In 1957, Ahrens [25] drew a relationship between iodine values of dietary fats and serum cholesterol levels. Compared to corn oil, fats such as lard, palm oil, butter, cocoa butter, and coconut oil were significantly more cholesteremic. Peanut oil yielded cholesterol levels similar to those observed with corn oil. When administered as part of an atherogenic diet, however, peanut oil was found to be inordinately atherogenic for rats, [26, 27] rhesus monkeys, [28, 29] and rabbits, [30] A mixture of fats whose fatty acid spectrum resembled that of peanut oil minus arachidic and behenic acids was no more atherogenic than corn oil, [30] but subsequent studies showed that randomization of peanut oil significantly reduced its atherogenicity. [31] Randomization is an interesterification process whereby the component fatty acids of a triglyceride are evenly distributed among the three glycerol positions. The experiments are summarized in Table 2. Randomization does not affect the atherogenicity of butter or lard. These findings suggest that more remains to be learned concerning fat structure and its effects on cholesterol metabolism and atherosclerosis. When added to a cholesterol-free, semi-purified diet, peanut oil is less atherogenic than either butter or coconut oil but is significantly more atherogenic than corn oil. [32]

PROTEIN

Ignatowski [33] provided the first clear demonstration that diet affected the course of atherosclerosis. He fed meat, milk, and eggs to rabbits and observed atherosclerosis lesions in their aortas. Ignatowski concluded that the animal protein had injured the aortic wall. However, all of the substances which he fed contained cholesterol, and the demonstration by Anitschkow and Cholatow [34] that diets containing cholesterol in vegetable oil could produce atherosclerosis shifted research emphasis towards cholesterol and other lipids.

TABLE 2.—INFLUENCE OF PEANUT OIL AND OTHER FATS ON EXPERIMENTAL ATHEROSCLEROSIS IN CHOLESTEROL FED RABBITS¹

Fat	Number of animals	Serum cholesterol (mg/dl)	Average atheroma ²	
			Aortic arch	Thoracic artery
Coconut oil.....	44/45	1,360	2.15±0.16	1.67±0.14
Peanut oil.....	98/106	1,483	1.89±.10	1.35±.08
PGF ³	73/76	1,650	1.57±.10	1.11±.09
PGF plus AB ⁴	31/31	1,723	1.40±.12	.94±.09
Peanut oil-R ⁵	31/31	1,833	1.31±.12	1.05±.10
Corn oil.....	100/106	1,548	1.52±.10	1.05±.07

¹ All diets contain 2 percent cholesterol and 6 percent fat.

² Graded on a scale of 0-4.

³ Prepared by blending 10 percent cottonseed oil, 55 percent olive oil, and 35 percent safflower oil. Fatty acid composition resembles that of peanut oil less arachidic and behenic acids.

⁴ PGF interesterified with arachidic and behenic glycerides. Fatty acid composition was identical with that of peanut oil.

⁵ Randomized (autointeresterified) peanut oil.

In comparing epidemiologic data relating to diet and heart disease, Yudkin [35] and Yerushalmy and Hilleboe [36] observed in 1957 that the incidence of ischemic heart disease could be correlated with intake of animal protein as readily as with intake of fat.

The data in Table 1 also suggest that the trend of increasing coronary mortality in the United States parallels the increasing ratio of animal to vegetable protein. The protein level of the American diet has been virtually unchanged since 1909. Although there has been little work reported on the effects of dietary protein on serum cholesterol levels and atherosclerosis, the available data suggest that both type and amount of protein may be important. In 1920, Newburgh and Squier [37] reported that rabbits fed a meat diet exhibited some atherosclerosis after 4 weeks; if the diet contained casein (30 g/day), aortas were normal at 10 weeks but did become atherosclerotic by 11 months. A later experiment [35] showed that rabbits fed powdered beef at a level sufficient to give a 27 percent protein diet showed atheromatous lesions after 1 year; no lesions were observed at 26 weeks. If the diet contained 36 percent protein, early atherosclerosis could be seen by 2 months. The only cholesterol present in the diet was that contained in the dried beef. Rabbits fed the 27 percent protein ingested about 30 mg of cholesterol daily. Meek and Kesten [39, 40] fed rabbits 250 mg of cholesterol daily in diets containing 38 percent casein or 39 percent soy protein or a basal diet. The soy protein diet gave the highest serum cholesterol levels but the lowest incidence and severity of atherosclerosis. When the rabbits were fed only 60 mg of cholesterol daily, the basal diet was more atherogenic than the soy protein diet. In the absence of cholesterol only the casein diet was found to be atherogenic.

Nath *et al.* [41] fed rats cholesterol and different levels of casein and wheat gluten and found that the former protein was the more cholesteremic. When it was 40 percent of the diet, casein gave an average cholesterol level of 431 ± 39 mg/dl, whereas the level in rats fed 40 percent wheat gluten was 210 ± 8 . Similar differences were observed at other levels of protein.

Lofland and his co-workers [42-45] fed pigeons and squirrel monkeys diets in which the fat and the amount and level of protein and cholesterol were varied. The results of one experiment are summarized in Table 3. They show that serum cholesterol levels vary with the type of fat and level of protein, but in general, the high-protein diets were more atherogenic than the low-protein diets. In other experiments, [43] they found that in the absence of dietary cholesterol a 15 percent protein diet was more atherogenic than either 30 percent or 5 percent protein diets, but when 0.25 percent cholesterol was added, the 30 percent protein diet became the most atherogenic. These findings held true whether the dietary fat was corn oil or coconut oil. When squirrel monkeys were fed high- or low-protein diets, the severity of aortic and coronary atherosclerosis was similar in the absence of cholesterol, but the high-protein diet was more than twice as atherogenic if cholesterol was added to the diet. Computerized statistical analysis of the data from all these experiments revealed no independent variable.

TABLE 3.—INFLUENCE OF FAT AND PROTEIN ON ATHEROSCLEROSIS AND SERUM CHOLESTEROL LEVELS IN PIGEONS¹

Fat	Wheat gluten		Casein	
	High	Low	High	Low
Butter:				
SC:-----	419+23	398+22	472+22	399+47
AI ² :-----	3.5 (100)	4.3 (60)	5.1 (89)	3.1 (71)
Corn oil:				
SC:-----	492+32	676+96	345+41	404+31
AI ² :-----	5.7 (78)	3.5 (56)	5.2 (100)	.1 (56)
Crisco:				
SC:-----	495+45	377+37	577+98	643+56
AI ² :-----	4.3 (85)	2.5 (58)	3.5 (89)	.7 (55)
Margarine:				
SC:-----	442+32	387+32	375+24	242+21
AI ² :-----	2.0 (60)	1.3 (36)	3.0 (73)	.4 (42)

¹ After Lofland *et al.*

² Figures in parentheses percent.

Note: High=30 percent of calories, low=8 percent of calories, SC=serum cholesterol (mg/dl), AI=atherotic index; prevalence in parentheses.

Strong and McGill [46] fed baboons diets high (20 percent of calories) or low (8 percent of calories) in casein, high (0.5 percent) or low (0.01 percent) in cholesterol and containing 40 percent of calories as saturated (iodine value, 53.0) or unsaturated (iodine value, 108.9) fat. Thus, there were eight dietary combinations: high cholesterol plus saturated or unsaturated fat and high or low protein and low cholesterol-saturated or unsaturated fat-high or low protein. In only one set (high cholesterol-saturated fat) did the low-protein diet lead to more aortic sudanophilia than did the high-protein diet. In the other three sets, the high-protein diet was more sudanophilic and cholesteremic. Statistical analysis of the cholesterol data showed significant interactions between lipid parameters and cholesterol and a significant second order interaction of protein with fat and cholesterol.

In chickens, low-protein diets enhance experimental atherosclerosis, [47] and high-protein diets appear to have a protective effect. [48, 49] Protein level does not affect spontaneous atherosclerosis in chickens. [50]

Munro et al. [51] found that rabbits fed 1 percent cholesterol plus 30 percent casein had more cholesterol in their adrenals (45 percent) and liver (148 percent) than did rabbits fed 1 percent cholesterol plus 8 percent casein. Serum cholesterol levels in the 30 percent protein group were 820 mg/dl compared with 605 mg/dl in the 8 percent protein group. Atheromata in the high protein group were slightly more severe (2.1 versus 1.7).

Howard et al. [52] found that replacing casein with soya flour inhibited the hypercholesteremia and atherosclerosis observed in rabbits fed semi-purified diets.

Hodges et al. [53] carried out an experiment in 6 volunteers who were fed diets containing various ratios of simple and complex carbohydrates. Their source of protein was mixed at the beginning and end of the experiment, but was soybean protein during the study. The average cholesterol level was almost 300 mg/dl at the beginning of the study, dropped to about 200 mg/dl during the test period and rose to the beginning levels when the diet reverted to a mixture of animal and vegetable protein.

Walker et al. [54] reported that young women ingesting a diet containing 50 g of vegetable protein had lower serum cholesterol levels than did women eating 50 g of animal protein.

Carroll and Hamilton [55] studied the effects of defatted protein (30 percent) on serum cholesterol levels in rabbits. They fed a number of proteins of animal and vegetable origin and found the latter type to be uniformly less cholesteremic (Table 4). Of interest in these experiments are the observations that potato starch can completely vitiate the hypercholesteremic effect of casein and that butter or corn oil plus either casein or soy protein yield lower cholesterol levels than when either protein is fed in a low-fat diet.

The foregoing suggests the need for awareness of possible interactions when assessing the effects of diet. Caution should be exercised before attributing cholesteremic or atherogenic effects to any one component.

CARBOHYDRATES AND FIBER

Yudkin [55, 56, 57] has put forward the hypothesis that sucrose consumption is of central importance to the etiology of ASHD. His views are based on a correlation of coronary heart disease mortality with sugar intake in certain countries. Yudkin's hypothesis has been subjected to criticism. [58-60] With regard to Yudkin's sucrose hypothesis and other theories implicating other single dietary components, it is well to remember Ashton's [61] caution against any direct causal interpretation of dietary correlations.

Dietary carbohydrate affects serum triglyceride levels [62-64] but appears to have little effect on serum cholesterol levels. [65] Grande [66] has reviewed the effects of carbohydrates on serum lipid levels and emphasized the complexity of the findings and the difficulties in interpretation. One should separate effects of simple carbohydrates from those of the more complex ones. Among the latter, sucrose and fructose are generally considered to be more triglyceridemic than

glucose, although there are conflicting data. Anderson [67] has reviewed some of these data.

Complex carbohydrates contain various levels of nonnutritive fiber, and the fiber, rather than the nature of the digestible sugar, may account for the reported differences.

TABLE 4.—EFFECT OF PROTEIN ON PLASMA CHOLESTEROL LEVELS OF RABBITS¹

Protein	Plasma cholesterol (mg/dl)	Protein	Plasma cholesterol (mg/dl)
Animal:		Raw egg white.....	100
Whole egg extract.....	232	Vegetable:	
Skim milk powder.....	228	Wheat gluten.....	82
Lactalbum.....	212	Peanut protein.....	82
Casein.....	204	Pea protein.....	46
Fish protein.....	166	Soy protein.....	40
Beef protein.....	158	Fava bean protein.....	32
Pork protein.....	112		

¹ After Carroll and Hamilton. Groups of 4 to 7 rabbits were fed a diet containing 30 percent protein and 1 percent fat or 28 days.

About 20 years ago, two groups of investigators [22, 23] reported that they had established atherosclerosis in rabbits by feeding them a diet free of cholesterol but high in saturated fat. Collation of the literature available at that time [68] indicated that the addition of saturated fat to a stock diet did not render it atherogenic, but that when the same fat was part of a semi-purified diet, that diet was hyperlipidemic, hyper- β -lipoproteinemic, and atherogenic for rabbits. Clearly, the fat alone was not the determinant of atherogenesis, and it was suggested that the type of carbohydrate or fiber present in the diet might be important. [68] An experiment was carried out in which a semi-purified diet containing 40 percent dextrose and 14 percent hydrogenated coconut oil was compared with a diet containing 85 percent lipid-free residue obtained by extraction of laboratory ration, 1 percent vitamin mix, and 14 percent hydrogenated coconut oil. [69, 70] The semi-purified diet was much more cholesteremic and atherogenic. Moore [71] carried out an experiment using a semi-purified diet containing 20 percent butter and varied the non-nutritive element of the diet (wheat straw; cellulose; cellophane; or cellophane:peat, 14:5). The cellophane-containing diet was most cholesteremic and atherogenic, followed closely by the cellulose diet. The wheat straw diet was least atherogenic.

Experiments with different types of carbohydrates in the semi-purified diet [72, 73] indicated that fructose and sucrose were much more atherogenic than glucose. Lactose was not atherogenic when a component of a cholesterol-free diet; although lactose (30 percent) plus cholesterol is severely atherogenic for rabbits. [74] Our data [72, 73] are summarized in Table 5.

Semi-purified diets containing different carbohydrates have been fed to baboons. [75] Fructose, sucrose, starch, and glucose are equally cholesteremic. Glucose and starch raised triglyceride levels by 43 percent, and fructose and sucrose raised them by 55 to 72 percent. The most sudanophilic carbohydrate was fructose and the least, glucose. A fructose-rich semi-purified diet was found to be atherogenic for vervet monkeys. [76] The mechanism of action of this type of diet

appears to involve decreased synthesis of bile acid, which results in reduced conversion of cholesterol in the liver and its diversion to the serum. [75,77,78]

When different carbohydrates are fed to animals on a cholesterol diet, sucrose is more cholesteremic than glucose for rabbits [79, 80] or chickens. [81, 82] Lang and Barthel [83] fed 0.5 percent cholesterol and 66 percent sucrose or dextrin to three different species of monkeys. In *Macaca mulatta*, dextrin was more cholesteremic and atherogenic, but aortic cholesterol was higher in sucrose-fed monkeys; in *Cebus albifrons*, dextrin gave more intimal proliferation of the coronary arteries but no higher cholesterol level; in *Macaca arctoides* there was no difference between the diets.

TABLE 5.—EFFECTS OF CARBOHYDRATES ON ATHEROSCLEROSIS IN RABBITS
FED CHOLESTEROL-FREE, SEMIPURIFIED DIETS¹

Carbohydrate	Serum cholesterol (mg/dl)	Average atheromata	
		Aortic arch	Thoracic artery
Experiment 1 ² (33 weeks):			
Glucose.....	209 ± 31	1.1	0.9
Sucrose.....	310 ± 66	1.9	1.0
Starch.....	640 ± 97	2.3	1.2
Hydrolyzed starch.....	400 ± 77	1.7	1.0
Experiment 2 ³ (40 weeks):			
Glucose.....	451 ± 102	1.1	.6
Fluctose.....	922 ± 231	2.1	.9
Sucrose.....	520 ± 0.19	1.7	1.2
Lactose.....	329 ± 144	.6	.4
Starch.....	532 ± 152	1.5	1.2

¹ All diets contain 40 percent carbohydrate, 25 percent casein, 15 percent cellulose, 14 percent hydrogenated coconut oil, 5 percent salt mix, and 1 percent vitamins.

² Kritchevsky et al.

³ Kritchevsky et al.

Most semi-purified diets contain cellulose as the bulking agent. Substitution of alfalfa in rat diets will inhibit cholesterol absorption, [84] and any number of mucilaginous gums will lower serum and liver cholesterol levels. [85, 86] Pectin will inhibit cholesterol-induced atherosclerosis in rabbits, [87] chickens, [88, 89] and pigs. [90]

The absence of atherosclerosis in many primitive peoples has been attributed to the high level of fiber in their diets. [91-95] Keys et al. [96] found that cellulose did not lower cholesterol levels in man but that pectin did. Bran has also been shown to have no effect on serum lipids in man. [97] Leguminous products such as bengal gram [98] have a marked hypocholesteremic effect in man (Table 6).

Experiments in which dietary sucrose has been replaced by some form of starch result in reductions in serum cholesterol levels ranging from 2 to 11 percent. Some of these are summarized in Table 7.

Interaction between dietary fiber and protein can affect atherosclerosis. We have fed rabbits semi-purified diets containing cellulose, sucrose, and casein or soy protein. The casein diet is more cholesteremic and atherogenic. Substitution of wheat straw for the cellulose does not affect cholesteremia but reduces atherogenicity of both diets. When the fiber source is alfalfa, cholesterol levels are reduced in both groups and atheromata are of equal severity. [106]

TABLE 6.—INFLUENCE OF BENGAL GRAM ON LIPID METABOLISM IN 20 PATIENTS¹

Diet	Serum cholesterol (mg/dl)	Fecal steroids (mg/24 hr)		
		Neutral	Bile acids	
			Cholic	Deoxycholic
Basal.....	123±23	272	59	105
High fat (10 weeks).....	206±20	455	74	163
High fat+Bengal gram (55 weeks).....	160±24	470	106	200

¹ After Mathur et al.

TRACE ELEMENTS

The possibility that trace elements may affect atherosclerosis is usually met with tolerant disinterest. While the data may not be as compelling as those involving the major dietary components, they carry a respectable epidemiologic imprimatur. In view of the increasing evidence of the importance of dietary interactions, trace elements may be important for their possible role in effecting those interactions.

Water softness has been implicated as an etiologic factor in cardiovascular disease. [107-109] Water hardness has also been negatively correlated with sudden death from arteriosclerotic heart disease or other causes. [110, 111] Masironi and his co-workers [112, 113] have summarized the findings in the United States as well as internationally; a summary of their findings is presented in Table 8. The correlation seems to be especially strong for hypertensive heart disease. [112]

TABLE 7.—EFFECT OF EXCHANGING SUCROSE FOR STARCH ON SERUM CHOLESTEROL LEVELS OF NORMOLIPEMIC PATIENTS

Study	Starch	Number subjects	Duration (days)	Calories exchanged (percent)	Change in serum cholesterol (mg/dl)	P	Reference
1.....	Fruit, vegetables, and legumes.....	28	42	17	-18±2.2	<0.01	99
2.....	Rice.....	6	25	19	-6±8.5	NS	100
3.....	Bread, potatoes.....	12	21	17	-4±5.7	NS	101
4.....	Leguminous seeds.....	12	21	17	-19±5.2	<.01	101
5.....	Cereals, potatoes ¹	18	28	23	-11±3.1	<.01	102
6.....	Cereals, potatoes ²	18	28	23	-10±4.2	<.05	102
7.....	Cereals, potatoes ³	18	28	23	-8±3.4	<.05	102
8.....	Bread.....	15	14	35	-13±8.1	NS	103
9.....	Bread.....	15	14	35	-24±7.0	<.01	103
10.....	Wheat starch ⁴	10	30	40	-9	-----	104
11.....	Wheat Flour.....	12	14	16	-7±4.4	NS	105
12.....	Mixed vegetables.....	12	14	16	-22±3.8	<.01	105

¹ Coconut oil.² Olive oil.³ Safflower oil.⁴ Studied in women only.

TABLE 8.—NEGATIVE ASSOCIATION BETWEEN CARDIOVASCULAR MORTALITY AND WATER QUALITY¹

Country	Number of studies	Main characteristics of water
Canada.....	2	Hardness.
Finland.....	2	Dissolved solids, conductivity.
Ireland.....	1	Hardness.
Italy.....	2	Do.
Japan.....	2	Hardness, alkalinity.
Netherlands.....	1	Hardness, Ca.
Sweden.....	1	Do.
United Kingdom.....	5	Hardness, Ca, Mg.
United States.....	8	Hardness, Ca, conductance, α and β radio-activity.

¹ After Masironi et al.

Muss [114] related water quality in each of the contiguous United States with deaths from cardiovascular disease. Table 9 shows that there is a general correlation; thus, the six states with the highest death rates range from 12th to 47th in water hardness, whereas the six states with the lowest death rates range from 1st to 10th in water hardness.

TABLE 9.—CORRELATION OF MALE CARDIOVASCULAR DEATH RATE WITH WATER HARDNESS

State	Death rate	Water hardness	State	Death rate	Water hardness
South Carolina.....	1	47	Montana.....	25	18
Maryland.....	2	36	Alabama.....	26	33
Nevada.....	3	14	Arizona.....	27	5
New Jersey.....	4	28	Mississippi.....	28	40
Illinois.....	5	12	Texas.....	29	15
Louisiana.....	6	30	Missouri.....	30	24
New York.....	7	35	Oregon.....	31	48
Pennsylvania.....	8	27	Wisconsin.....	32	11
North Carolina.....	9	41	West Virginia.....	33	26
Rhode Island.....	10	42	Tennessee.....	34	29
Massachusetts.....	11	44	Idaho.....	35	19
Georgia.....	12	39	Kentucky.....	36	25
California.....	13	20	Utah.....	37	7
Florida.....	14	17	Oklahoma.....	38	16
New Hampshire.....	15	43	Iowa.....	39	6
Virginia.....	16	31	Minnesota.....	40	22
Delaware.....	17	32	Arkansas.....	41	38
Indiana.....	18	4	Colorado.....	42	23
Michigan.....	19	21	Wyoming.....	43	9
Connecticut.....	20	45	Kansas.....	44	8
Ohio.....	21	13	Nebraska.....	45	2
Washington.....	22	37	South Dakota.....	46	1
Vermont.....	23	24	North Dakota.....	47	10
Maine.....	24	46	New Mexico.....	48	3

Voors [115] suggests that the beneficial effect of water hardness should be viewed in the light of the high positive correlation between water hardness and lithium level.

Schroeder [116] has suggested that chromium deficiency is a factor in atherosclerosis. His suggestion is based on analyses of chromium in

tissues of Americans of different ages and comparison with data from tissues available from abroad. In the United States, chromium levels in aortas and livers fall with increasing age, and atherosclerotic aortas may contain no chromium at all. Chromium is essential for glucose and lipid metabolism [117] and its lack may increase atherosclerosis. The best sources of dietary chromium are brown and raw sugars, millet, beets, and peas.

Klevay [118] has raised the possibility that coronary heart disease can be explained in the ratio of dietary zinc to copper, a high Zn/Cu ratio being detrimental. He has reviewed the epidemiologic literature and concluded that the Zn/Cu ratio is more closely associated with risk than any factor save cholesterol. Klevay has shown [119] that there is a high Zn/Cu ratio in high fat foods and suggests that the efficacy of dietary fiber [120] lies in the fact that the phytic acid of fiber ties up excess zinc. In experiments with rats, [121] Klevay has shown that conventionally reared rats fed a diet with a Zn/Cu ratio of 5 have cholesterol levels of 141 mg/dl, whereas the cholesterol level is 180 mg/dl if the ratio is 40. It will be interesting to follow this work through a series of dietary experiments. Human autopsy material and tissues from animals maintained on various atherogenic diets should yield important clues relating to the Zn/Cu hypothesis.

In summary: There is much to be learned about the effects of dietary interactions on serum lipid levels and atherosclerotic heart disease. Although fat intake has been most commonly indicated as the causative agent in heart disease, other dietary components can affect serum lipids. Attempts to correlate death rates from ASHD with cholesterol intake lead to some anomalous data. [122] Thus, in 1955 to 1956 the USA had the highest death rate (750/100,000) and an average cholesterol intake of 600 mg/day. Finland, with the second highest death rate (680/100,000), showed a cholesterol intake of only 310 mg/day. France, with a daily cholesterol intake of 350 mg had a death rate of only 140/100,000. These data were for men aged 55 to 59.

The amount and type of carbohydrate and protein affect serum cholesterol levels and atherosclerosis. Dietary fiber may also affect lipid levels. At this writing, the term fiber covers a variety of substances containing various amounts of celluloses, hemicelluloses, pectins, and lignins. Full understanding of the effect of fiber will come when we know the composition of the fiber present in each food and how each of these components affect metabolic processes. Finally, there is evidence that trace elements may exert an important effect on lipid metabolism. And not only may the elements per se be important but the ratio of one to another must be considered.

Recently, Armstrong et al. [123] have tried to relate commodity consumption and dietary practices in 30 countries to mortality from ischemic heart disease. They found positive correlations with gross national product, calories, animal and total protein, fat, sugar, meat, eggs, coffee, tea, and cigarettes. Negative correlations with cereals and vegetables were discerned. There were numerous first and second order correlations. They conclude: "These results suggest that associations identified in this type of investigation should be interpreted with great caution and need not necessarily reflect casual relationships but rather suggest avenues along which further research might proceed." Amen.

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TEXAS A. & M. UNIVERSITY,
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HON. GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs, U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: Allow me to congratulate you and your committee on your report, "Dietary Goals for the United States." With one exception, the report is objective and the recommendations justified. The one exception is the recommendation that the public, indiscriminately, reduce its saturated fat and cholesterol intake and increase its ingestion of polyunsaturated fat.

This recommendation should be limited to persons who are inclined for one or more of a number of reasons, to have high levels of lipid (fatty) substances in their blood. Since each of these persons needs different advice, depending upon the kind and degree of their disease, a general recommendation could do more harm than good. Furthermore, these persons constitute a small minority of our population.

When your committee report appeared I was writing a paper on the subject. I am enclosing a copy of the manuscript for your consideration.

It is obvious that the committee has been advised by a group that

has been able to see only one set of data on this problem, being overly influenced by epidemiological studies which have consistently failed to note that averages of normal people with abnormal people should not be used to advise the normals. The two groups must be considered separately. I have developed this point in my paper.

I trust that your committee will weigh my enclosed review, along with those of Dr. E. H. Ahrens and Sir John McMichael, which I have been privileged to read, and will modify your statement on the subject accordingly.

I am enclosing my biographical sketch. Note that I have worked and taught for 40 years in various aspects of lipid chemistry, metabolism and nutrition, having published over 140 research papers in peer-reviewed journals. I have no bias for or against any food type. As a scientist, rather than a physician, I am in a neutral position in this matter and qualified to judge the data.

Very truly yours,

RAYMOND REISER,
Professor Emeritus.

Enclosure.

OVERSIMPLIFICATION OF DIET: CORONARY HEART DISEASE RELATIONSHIPS AND EXAGGERATED DIET RECOMMENDATIONS*

(By Raymond Reiser, Department of Biochemistry & Biophysics, Texas Agricultural Experiment Station, College Station, Tex.)

ABSTRACT

The data relating diet to coronary heart disease, when critically examined, clearly show that there is a normal spectrum of blood serum values, and that normal persons do not develop pathological levels upon the ingestion of eggs and other cholesterol-containing foods. The data also show that the persons in only a small fraction of any population have pathological levels upon the ingestion of large amounts of cholesterol-containing foods. It is shown that average data obtained from mixed populations with normal and pathological blood lipid values should not be used to advise the normal majority of that population. The harmful effects of such policy are outlined. The concept that the risk of coronary heart disease is a function of serum lipids at any level is reviewed and found invalid. The data of the National Cooperative Pooling Project of the American Heart Association is used to show that up to 250 mg/dl there is no relationship between serum cholesterol concentration and risk.

The recent Federal Trade Commission hearings on advertising of fat and cholesterol-containing foods and the report of the Senate Select Committee on Nutrition and Human Needs, "Dietary Goals for the United States" [1] are reminders of the uncertainties in the public mind over the value of these foods.

With over a million coronary heart attacks and over 600,000 coronary heart attack deaths a year in the United States, a large percentage of which are of middle-aged men, it is indeed imperative that all steps be taken to reduce this loss. However, it is just as imperative that

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no action be taken which may be self-defeating and may do more harm than good. While the limitation of diet cholesterol to 300 mg per day [2] may be helpful to some people, it would give a false sense of security to others who need more sophisticated treatment. The inference of the advice to everyone is that all persons would thus reduce their risk of coronary heart attack. The inference is not true. The rationalization that it is not wrong to mislead normolipidemic persons in order to reach the hyperlipidemic ones on the grounds that it can do them no harm, is not only specious but it is fatuous as well. It is both misleading and paternalistic. The advice deprives the majority of people their most desirable, traditional, and protective foods: eggs, dairy products, liver, beef and pork, and even hydrogenated shortening and lard. It is difficult enough to teach the public to consume a balanced diet even with these items. In addition, it places unnecessary and unfair burdens on several major branches of agriculture and reduces the sources of much needed food.

Hyperlipoproteinemia is a disease syndrome and should be treated as such. Like diabetes, each victim needs individual treatment.

Almost 70 years have passed since it was first announced that including cholesterol in the diet of rabbits produced hypercholesterolemia and severe atherosclerosis. Millions of dollars have been spent with incalculable number of man-hours, of animals, of human subjects, and of printed reports, but the controversy over the relationship between cholesterol and other lipids in the diet, blood lipids, atherosclerosis, and CHD goes on.

That there is a relationship of some kind cannot be denied. Based on the positive data, a philosophy of prudence developed which has led the Intersociety Commission for Heart Disease Resources of the AHA to recommend in 1970 an immediate nationwide change in dietary habits for persons of both sexes and of all ages [2]. Two years later a more conservative statement was issued by the American Medical Association (AMA) Council on Foods and Nutrition jointly with the Food and Nutrition Board of the National Academy of Sciences-National Research Council that "Persons falling into 'risk categories' on the basis of the plasma lipid levels be made aware of this and receive appropriate advice. Such advice may vary somewhat with the blood lipid profile" [3]. The emphasis on the individual rather than the same advice to everyone has been stressed [4].

Contrary to the position of the AMA, the AHA, through every segment of the press, television, literature of various kinds mailed to physicians, and editorials in medical journals, pressed hard on the suspected dangers of "saturated fat" and cholesterol-containing foods, not discriminating between persons on the basis of their "blood lipid profile" as recommended by the AMA.

The manufacturers of margarine, egg and meat substitutes, and other segments of the food industry have taken full advantage of the AHA campaign and, in fact, have taken over the burden of indiscriminately weaning the public away from eggs, beef, pork, and dairy products containing butterfat. By constant repetition in all advertising media they have made it appear as a truism that anyone who consumes animal products, including meats, eggs, and dairy dishes, is in danger of CHD, and that substitution of *their* products will prevent the disease. They have made cholesterol appear to be a toxic substance similar

to dangerous additives. Margarine, egg substitutes, and meat substitutes, properly made, are good foods but should be sold on their merits of taste, physical qualities and price, not as medicines.

The official position of the AHA is contained in a February 13, 1976 statement signed by Daron Bryant, Chief of Public Policy and Government Affairs, which was presented to the Federal Trade Commission during its recent hearing on fat, fatty acids and cholesterol claims in advertisements. The burden of the AHA position herein stated, is that it does not think "the mere mention of a food which is 'low in cholesterol' or 'low in saturated fat' overemphasizes the role that food plays in reducing serum cholesterol levels", and supports the position that everyone should eat as though he/she is prone to be a hyperlipidemic.

The AHA statement repeats the 1970-72 recommendation of the Intersociety Commission on Heart Disease Resources for the reduction of dietary cholesterol to less than 300 mg per day for everyone. The statement goes on to say: "Assuming a caloric intake of 2,500 calories per day the average American should take in no more than 250 calories or less than 27 grams of saturated fat per day". Saturated fat is not defined. There is no "average American." The phrase is bound to be interpreted by any individual as meaning him or her, and thus, in practice, every American.

During this process of educating the public to consume "prudent" diets, and of castigating the so-called saturated fat and cholesterol containing foods, the fact that there is much evidence contrary to the universal applicability of the saturated fat-cholesterol hypothesis has been lost sight of. The advertising campaigns have been so intense and so persistent that the word cholesterol has become almost synonymous with coronary heart disease in most people's minds, including not only the man in the street but many physicians and even nutritionists and other scientists. There is an inference in this publicity and the advertisements that coronary heart disease will go away if everyone will substitute vegetable polyunsaturated oil for saturated fat and cholesterol containing foods, and yolk-free egg whites for whole eggs. It has been forgotten that the evidence is conflicting and that in the beginning the "prudent" diet was intended as a temporary measure until the conflict could be resolved. The scientific world is as susceptible to oft-repeated statements as is the most untutored layman. For example, one of blanket recommendations is repeated as a major point in the report of the Select Committee on Nutrition and Human Needs of the United States Senate, the so-called McGovern Report [1].

But more data are becoming available, and these data along with the passage of time permit us to take another look at the old data with a fresh perspective. It is quite possible that the conflict among the old data can now be reinterpreted and the anomalies explained.

Close examination of accumulated data shows what has been clear all along, even to the sponsors of the diet-heart theory: Hyperlipidemia and its sequellae are symptoms of a number of diseases with multiple causes, both genetic and environmental. What has been underemphasized and even overlooked, at least understated, is that everyone doesn't have the symptoms, that those who do require individual treatment other than diet, and that the majority of the general public have benign levels of serum cholesterol on any diet.

This phenomenon is a tangled skein. There is an inference that everyone has the potential for the disease and all he has to do to get it is to eat eggs, meat and butterfat. The fact that there are individual variations in the blood lipid response to diet variables is well known but ignored in diet recommendations, especially those by food advertisers.

It is true that everyone's serum lipids will respond to diet variables to some degree. The big question is, is there a spectrum of benign levels or is the risk of coronary heart disease directly related to serum lipid concentrations at all levels of response to diet?

Since lipids are normal serum constituents the question is, where do normalities stop and pathological or atherogenic levels begin?

There are a few reports in which it is claimed that the relationship between the risk of coronary heart disease and serum cholesterol concentration is continuous at all levels. One [5] is a statistical analysis of the Framingham data up to 1962 which the author interpreted to mean that for each 1 percent increase in serum cholesterol concentration at any level the risk of coronary heart attack increased 2.66 percent. However, an 8-year later and more complete evaluation of the Framingham data by the official statistician of the study was that the data showed no relation between diet variables and CHD [6]. If these conclusions are both true, that is, diet does not affect risk but any change in serum cholesterol does, one must conclude that diet has no effect on serum cholesterol concentration at any level. This is certainly not true. However, the anomaly may be resolved if it can be shown that dietary differences may modify serum cholesterol concentrations within benign levels in normal persons and within pathological levels in hypercholesterolemic persons, but will not always increase benign to pathological concentrations.

In 1974 Mr. Tavia Gordon in a private communication to Dr. William B. Kannel, Director of the Framingham Study, referring to the relationship between serum cholesterol and risk wrote, "We have no proof that anyone would lower his chances of developing CHD by reducing his serum cholesterol level, whether that level be 220 or 320 or whatever. The truth is, however, that we would need many more observations than we have to be able to assert from experience that at very low levels an increment of risk with increased serum cholesterol really occurs".

A second study which, at first glance, would appear to support the concept that the risk of CHD is directly related to serum cholesterol concentration at all levels is that of Carlson and Bottinger [7]. Linear regression analysis of new events of CHD of five quintiles of serum cholesterol levels of men under 60 years of age gave virtually a linear relationship. In men over 60 years of age there was no relation between CHD and serum cholesterol. It was overlooked that serum cholesterol and CHD both increase with age under 60 years. Thus to demonstrate the true relationship with serum cholesterol and risk, each age group must be treated separately.

Perhaps the best evidence refuting the concept that each increment of serum cholesterol, regardless of how low the level, carries an added degree of risk is the National Cooperative Pooling Project of the AHA [8]. The data from this summary of eight long-term studies of adult cardiovascular diseases show no real difference in risk among

persons with serum cholesterol below 250 mg/dl (Fig. 1), about 5 per 1,000 per year. It is probable that these five incidents were due to factors other than serum lipids which may generate coronary occlusion and infarct. Of the group with serum cholesterol levels between 225 and 249 mg/dl, 6.7 persons per 1,000 per year experienced their first coronary event. This is 1.7 persons per 1,000 above the basal 5. Considering the poor degree of reproductibility of such studies and the absence of any confidence values in the statistics, such small differences in risk between this group and those with lesser serum cholesterol concentrations is also "too trivial to be concerned about". That is, there is no difference in risk among persons with serum cholesterol values below 250 mg/dl. According to these data, which are the best available, there are three levels of risk vis-a-vis serum cholesterol: 5 per thousand per year with serum cholesterol below 250 mg/dl; 11 thousand per year with serum cholesterol between 250 mg/dl and 299 mg/dl; and 16 per thousand per year with serum cholesterol values above 300 mg/dl. Such data do not support the theory that risk increases with each increment in serum cholesterol concentration.

It is pertinent that The Committee on Diet and Heart Disease of the National Heart Foundation of Australia, in a position statement [9] concludes: "Dietary modification should be considered for subjects whose serum cholesterol level exceeds 250 mg/100 ml, or whose serum triglyceride level exceeds 160 mg/100 ml. Since at least one-third of middle-aged men and women are hyperlipidaemic by these criteria, measurement of serum lipids in all adults should be encouraged".

That there are nonatherogenic and atherogenic levels of lipidemia can hardly be denied. The prefix "hyper-" makes "normo-" an unavoidable corollary. Lipids are certainly normal constituents of blood serum, therefore they cannot be disease producing at all levels.

In their classical series on the classification of the hyperlipidemias, Fredrickson et al. [10] repeatedly referred to "normal" and "hyper-" levels, clearly reserving the latter for abnormal or disease levels and the former for nondisease levels. Fredrickson, in another place [11], emphasized the distinctions between "the normal pattern" and "abnormal patterns".

Clearly one must make a distinction between humans who are hyperlipidemic and those who are not, and explain that these can be sorted by blood chemistry: "The simplest screening method is a measurement of the total lipid content of plasma" [10]. The authors list what they consider to be the "plasma lipid and lipoprotein concentrations of normal subjects". Quoting only the mg percent total cholesterol values, they are, according to age and sex:

	Years of age				
	0-19	20-29	30-39	40-49	50-59
Male.....	172±34	183±37	210±33	230±55	240±58
Female.....	179±33	179±35	204±37	217±35	251±49

The 50-59 age values conform to the adult values of the National Pooling Project [8]. These values are also in agreement for men with those of the Vital and Health Statistics U.S. 1960-62. The values for females are lower than those in U.S. Statistics [12].

Fredrickson et al. [10] mention two subdivisions of primary hyperlipoproteinemia (not related to other diseases such as diabetes), familial (heritable) and sporadic. While no one questions that the familial type is an abnormality, one finds almost no serious discussions of the "sporadic", nor do Fredrickson et al. define it further. The term can apply to the sporadic appearance in some people, or to the occasional appearance in everyone.

It is agreed that different humans on the same diets will have a spectrum of serum cholesterol concentrations from below 150 mg/dl to extremely high levels. There is also agreement that in some individuals these levels will be differently affected by changes in diets than in others. Some, regardless of diet, will remain in indisputably benign levels. Others will remain in indisputably high levels. A third group may have benign levels on low fat-low cholesterol diets which may increase to levels which carry added risk upon the ingestion of high fat and cholesterol diets, all other risk factors remaining constant.

It must be to the third group to which the recommendation to restrict diet cholesterol should be addressed. The second group, those with inadvisably high serum cholesterol levels on any diet, have a disease and must be treated individually.

If these conditions are true, the only possible justification for advising everyone to restrict diet cholesterol would be if the third group is overwhelmingly large. But how large is it?

The value is different in different age groups. Wood et al. [13] found that the following percentages of humans had serum cholesterol concentrations equal to or greater than 240 mg/dl and 275 mg/dl in 494 normal men and 503 normal women, respectively. Normal was described as those having no diabetes nor electrocardiograph abnormalities, and with diastolic blood pressure below 100 mm Hg.

	Men		Women	
	More than 240 milli- grams daily	More than 275 milli- grams daily	More than 240 milli- grams daily	More than 275 milli- grams daily
Age range:				
40 to 49.....	17	4.1	15	3.1
50 to 59.....	29	6.7	36	9.2
60 to 69.....	30	8.3	36	15.0

As explained above, according to the National Pooling Project [8] persons with serum cholesterol above 275 mg/dl are hypercholesterolemic. Those with serum cholesterol below 250 mg/dl are not at increased risk. From the data of Woods et al. [13] it may be calculated that 68 percent of the 7494 persons in the study had serum cholesterol below 250 mg/dl.

Referring to the U.S. Vital Statistics [12] 61 percent of males between ages 45 and 54 have serum cholesterol concentrations less than 240 mg/dl and 86 percent below 280 mg/dl. By extrapolation, 67 percent have serum cholesterol values below the critical 250 mg/dl, the same as calculated from the Pooling Project data. Thus 25 percent are between the benign and increased risk levels and might benefit by a low cholesterol diet.

Thus, by the best data, only about 30 percent of men in their most critical years may develop increased risk levels of serum cholesterol.

Since not less than 5 percent are not controlled by diet alone, a maximum of 25 percent of men at the most susceptible age would benefit from the recommendation.

In most epidemiological studies relating diets, blood lipids, and atherosclerosis and/or CHD two factors are often not adequately considered. One is the diets of the individuals, which may be very different during the month or two preceding the experiment. The other is the failure to statistically separate hypercholesterolemics from normal. Data thus obtained are mean values of a population and truly apply to only a limited number of individuals.

An example is the study *Coronary Heart Diseases in Seven Countries* [14]. Although one of the main objectives of this study was to relate diet to CHD, and a limited effort was made to determine diet intakes, data are not given for cholesterol intake and therefore no relationship of diet cholesterol to serum cholesterol or to CHD can be drawn. All emphasis was on undefined "saturated fat" and total calories. Nonresponders, responders, and true hypercholesterolemics were included as normal variations in an homogeneous population. There is no homogeneous population in this sense. Uncritical examination of a figure in that report (xvii.4) appears to demonstrate a straight line relationship between serum cholesterol and risk. However, closer examination shows how the data may be interpreted alternatively. The natives of 6 of the 13 places studied have exactly the same serum cholesterol concentrations. That alone should make any conclusion relating serum cholesterol values to coronary events questionable. Additionally, the incidence of CHD in the 6 places varies from about 0.5 to 6 persons per 100 over a 5-year period. Yet, except for East Finland, the highest incidence found was only a little over 8 per 100 in the 5 years, and in 11 of the 13 places only 7 per 100. A reasonable explanation for the relationships which do exist is that the higher risk groups contain more persons with hyperlipoproteinemia. The groups could be different genetically in this regard: Finns, Yugoslavians, and U.S. Railroad Men.

The dangers attendant to this type of study, and the impossibility of determining incidence rates from studies of poorly defined (unhomogeneous) populations have been clearly pointed out [15]: "... it is not possible to tell from uncontrolled samples (of populations) whether an observed association between the incidence rate of ASHD (atherosclerotic coronary heart disease) and serum cholesterol is or is not, in substantial part, due to the uncontrolled factors." "... comparability of such death rates (coronary heart disease deaths) between countries with widely different medical and cultural standards is obviously highly questionable." It is interesting that these cautionary words were written eight years before publication of the *Coronary Heart Disease in Seven Countries* report [14].

An often-quoted study which, from one point of view, would appear to demonstrate a clear-cut difference in CHD deaths between person who consumer whole milk and butter and those who consumed filled milk and margarine is that of Miettinen et al. [16]. Serum cholesterol concentrations in men in one mental hospital (N) were

reduced from 268 mg/dl to 217 mg/dl by the filled milk and margarine diets, and from 268 mg/dl to 234 mg/dl in another hospital (K). In 12 years the percentages of CHD deaths were 0.57 percent (20 persons) and 1.30 percent (52 persons) respectively in the low cholesterol test and control groups in hospital N, and 0.75 percent (14 persons) and 1.51 percent (24 persons) in hospital K.

The serum cholesterol levels of the subjects at entry are not given, nor are they given separately of those who died and those who lived. It might well be that those who died were the hypercholesteroleemics and responded to the higher cholesterol containing diets, and those who did not die were the normocholesteroleemics and were minimally affected by the diets. The two values in hospital N, 0.57 percent and 1.30 percent, are almost identical respectively to the incidence of attacks in persons with serum cholesterol concentrations below 250 mg/dl and above 300 mg/dl in the Pooling Project [8].

Two additional points to consider in evaluating this study are: (1) The total cholesterol consumption, or even the consumption of other cholesterol containing foods besides the milk and butter, such as eggs, is not mentioned and (2) the incidence of nonlethal coronary heart attacks is omitted.

Because of the publicity given to the saturated fat-cholesterol theory and the prestige of the AHA, the public gets the impression that most experiments and epidemiological studies favor the theory. This is not so. The Framingham data were discussed above. The very recent report of the Tecumseh study [17] concludes with the statement, "Cholesterol and triglyceride levels were unrelated to quality, quantity, or proportions of fat, carbohydrate, or protein consumed in the 24-hour recall period".

There have been numerous reports of a failure of the serum of free-living persons to respond to the addition of eggs and other cholesterol-containing foods to their normal diet. Nestel reported having given eggs and other cholesterol containing foods to low cholesterol-consuming natives of New Guinea up to 1 percent diet cholesterol without a significant change in serum cholesterol [18].

In comparing eggs containing unusually high levels of polyunsaturated fat with normal eggs, Brown and Page [19] found that "normocholesteremic" men had an average serum cholesterol level of 174 mg/dl after 18 days without eggs in the diet and 203 and 212 mg/dl after 18 days of consuming 2 per day of either the ordinary fat eggs or polyunsaturated fat eggs. Thus, there was no statistical difference between the values after consumption of the two types of eggs. There were statistical differences between the values after the zero-egg and the two-egg periods. This is an excellent example that statistically significant differences and physiologically significant differences are not the same. There are no hard data demonstrating higher risk at 203 and 212 mg/dl than at 174 mg/dl.

Porter et al. [20] added one egg a day to normal mixed but very low cholesterol diets of 120 male volunteers for three months. There was no significant difference in the serum cholesterol concentration.

Slater et al. [21] studied two age groups (20-28 years and 39-66 years) of men with normal blood pressures who regularly ate eggs.

After determining their serum cholesterol while consuming normal diets, two eggs a day for two weeks were added to the diets of the younger group. All egg consumption was then stopped for two weeks. The older men, after the two-week control period, added one egg a day for four weeks then two eggs a day for an additional four weeks. This was followed by a two-week period of no eggs. There was no significant difference in serum cholesterol concentration between any two time periods.

As early as 1960, Brown and Page, were able to conclude after years of study with persons consuming various diets of natural constituents that "Dietary treatment was relatively effective in patients with hyperglyceridemia and mixed hyperlipemia but relatively less effective for those with hypercholesterolemia. These results suggest that the physician should know the patient's type of serum lipid abnormality in order to prescribe dietary treatment with reasonable assurance of the outcome" [19].

One could quote almost endlessly reports of positive or negative responses to diet cholesterol. It is noteworthy, however, that the positive responses, though statistically significant, usually remained within the benign levels if the initial levels were low. Two examples are those of Connor et al. [22] and Erickson et al. [23]. In both of these studies, using formula diets with normal prisoners, large dietary differences in polyunsaturated/saturated fatty acid ratios had no effect on serum cholesterol concentrations, but the addition of 250 mg of cholesterol a day from eggs and beef (Connor et al.) or from 6.4 percent egg yolk (Erickson et al.) did increase serum cholesterol from about 174 mg/dl to 202 mg/dl and 213 mg/dl in the Connor study and from 195 mg/dl to 217 mg/dl in the Erickson study. What is important in these values is that statistically significant increases in serum cholesterol concentrations caused by diet did not result in physiological differences. The diet cholesterol did not raise serum cholesterol to pathological levels. Note that these values are identical to those of Brown and Page in a similar study [19].

The differences reported in the effects of dietary cholesterol can have a number of explanations: One of these is the differences between semipurified diets and diets containing natural foods. The effect of phytosterols in reducing serum cholesterol has long been known. We have found that when dissolved in oil, as little as 0.25 percent mixed soy sterols can mitigate the hypercholesterolemic effect of 0.5 percent cholesterol in a semipurified diet, probably by inhibiting cholesterol absorption. (Fig. 2).

It has been shown more recently that pectins also reduce serum cholesterol, probably by chelating with bile acids and preventing their absorption. No one knows what other natural food constituents, even though not absorbed, may have similar effects.

Another factor is the differences in the populations under study. It has been assumed that the populations were homogeneous. Actually, all populations are made up of mixtures of various kinds, nonresponders, intermediate responders and responders. Some studies have been made with persons with a history of CHD, and others with these

and hypertensives carefully removed. The study, Coronary Disease in Seven Countries [14] as discussed above, assumed that differences in incidence of CHD and serum cholesterol concentration were due solely to saturated diet fat, yet they concerned populations with very different genetic backgrounds with, in all probability, different mixtures of normal, hypercholesterolemics, and the intermediate responders, those with serum cholesterol levels below 250 mg/dl on a low cholesterol diet but above 250 mg/dl on a high cholesterol diet.

The National Heart, Lung, and Blood Institute's Coronary Primary Prevention Trial now underway could further confuse an already clouded picture. Thirty-eight hundred persons are participating. All were judged to have Type II hyperlipoproteinemia with blood cholesterol levels of 265 mg/dl or more, according to an HEW news release of August 26, 1976. The subjects will be placed on low cholesterol, low saturated fat diets and treated with cholestyramine for 7 years.

It is predictable that the treatment will reduce blood cholesterol levels, and may well "prevent or slow down the development of premature coronary heart disease and its consequences—primary heart attacks". By definition these trial subjects have a disease and are hyperlipoproteinemic. It has already been established that more persons with serum cholesterol levels above 265 mg/dl will suffer heart attacks than those below 250 mg/dl. The danger lies in the interpretation of the results which could be quoted as proving that reducing the amount of fat and cholesterol in the diet will reduce the incidence of CHD. The fact that these were hypercholesterolemic persons and not persons with benign levels of blood cholesterol could easily be lost sight of. Yet the critical point of the question is whether everyone should be advised to limit his cholesterol intake.

The study that is needed is one with persons having serum cholesterol at the benign levels on a normal diet, and to determine whether adding to or removing the cholesterol from their diet increases or decreases the incidence of CHD.

The Coronary Primary Prevention trial is only with men. It has been demonstrated repeatedly that diet does not affect the incidence of CHD in women in spite of the fact that their blood cholesterol usually is higher than in men, especially after menopause. An example is the Minnesota Coronary Survey [24]. This fact has been ignored in recommendations to the public and especially in margarine advertisements.

A study in this laboratory (in press) shows clearly the effects of saturated and polyunsaturated fat, cholesterol, and plant sterols in a responding and nonresponding animal even though it includes the BHE rat (Fig. 2).

The fats used were lard and safflower oil, molecularly distilled to remove the sterols. Note that the stripped lard and safflower oil at 15 percent of the diet (about 30 percent of calories) had little effect on the serum cholesterol in male or female above that of the very low fat diet. The addition of 0.5 percent cholesterol dissolved in the fats

dramatically increased the levels of serum cholesterol although there are some very significant sex differences. The level in the male was doubled to about 200 mg/dl but remained in what should be considered the nonpathogenic level in humans. The levels in the females increased about five times to the 450–500 mg/dl range. Thus the male BHE rat might be considered a nonresponder and the female a responder.

The levels were significantly higher in the lard-fed animals than in the safflower-fed animals, but nevertheless, both diet groups of the same sex remained in the same physiological range. The addition of only 0.25 percent plant sterols, equal to only half of the cholesterol supplement, almost prevented the hypercholesterolemic effects of the cholesterol. Had pectin been added to this semipurified diet in addition to the plant sterols, the cholesterol effect may have been completely wiped out.

Preliminary results of another study underway in our laboratory show that a pronounced increase in serum cholesterol produced by the addition of cholesterol in beef tallow to a semipurified diet was greatly reduced by the further addition of plant pectins or animal mucopolysaccharides, demonstrating the sensitivity of the female Sprague-Dawley rat used. However, the addition of cholesterol containing foods with the same level of cholesterol, 0.5 percent of the diet, to low cholesterol containing, well balanced human type diets had no effect on serum cholesterol.

Considering the recent studies in which humans or rats consuming their natural diets gave no physiologically significant response to added eggs, and such studies as these in which plant sterols and pectins mitigated any increase in serum cholesterol due to cholesterol in the diet, it becomes clear that only hypercholesterolemics need beware of cholesterol containing foods.

One must conclude that present knowledge is adequate to recommend that the general public does not need to change its diet, but the hypercholesterolemics need to be screened and given individual treatment, the same as should be done for diabetes or any other disease with a diet factor.

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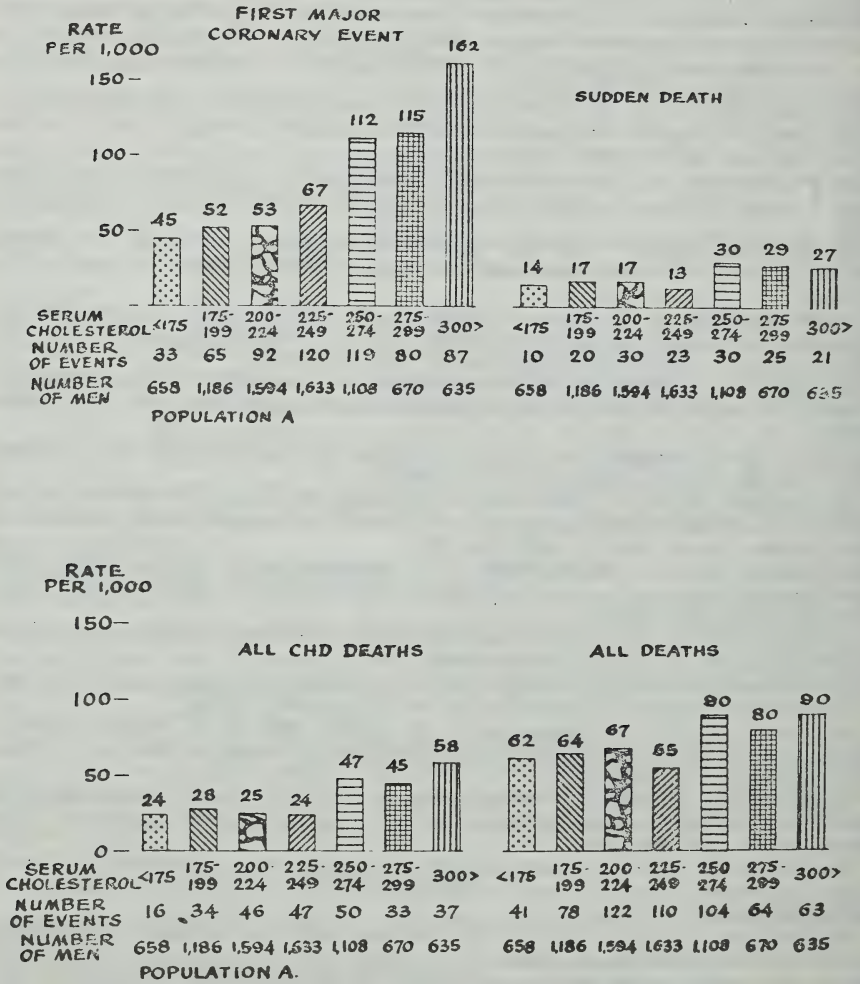
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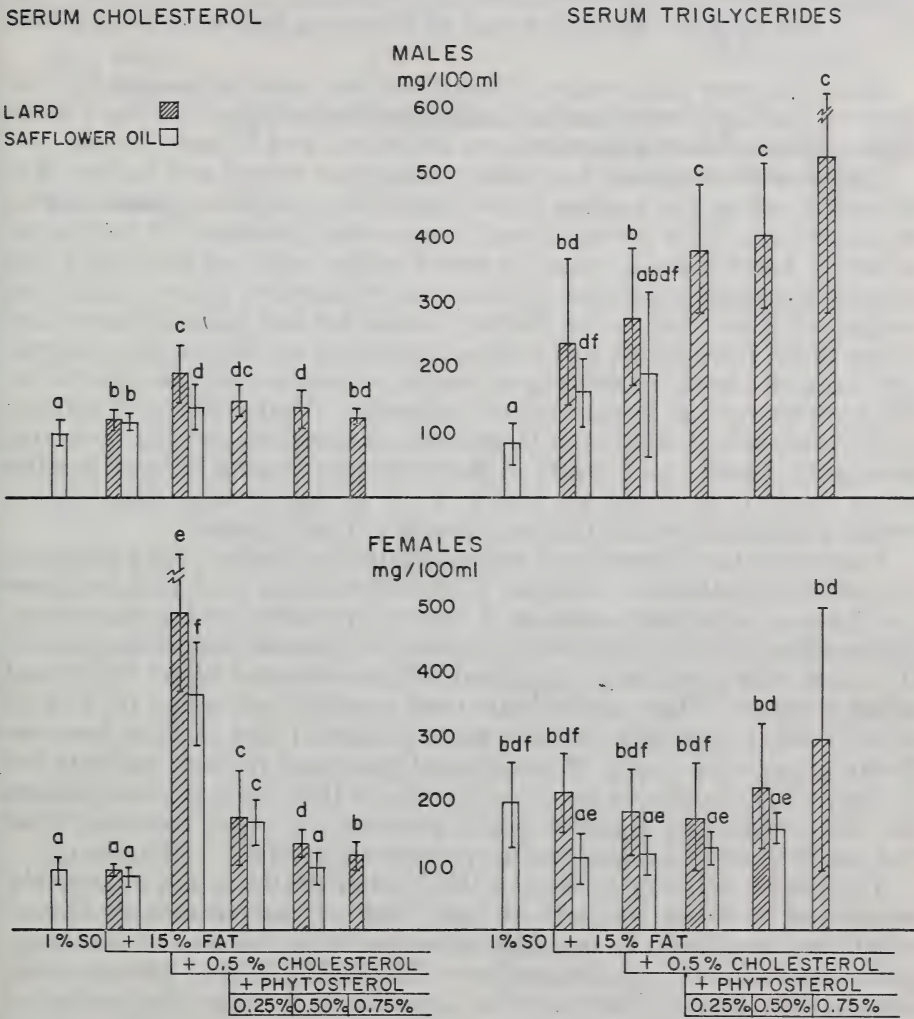
24. Frantz, I. D., Jr., E. A. Dawson, K. Kuba, E. R. Brewer, L. C. Gatewood and G. E. Bartsch. Minnesota Coronary Survey: Effect of diet on cardiovascular events and deaths. *Circulation. Suppl. II, Absts.* 51 and 52, 1975.

Figure 1: Serum cholesterol level at entry of 30-59 year-old men and 10-year adjusted rates of CHD per 1,000 men.



National cooperative Pooling Project; serum cholesterol level at entry and 10-year age-adjusted rates per 1,000 men for: any major coronary event, sudden death (upper graph), any coronary death, death from all causes (lower graph); any major coronary event includes non-fatal MI, fatal MI, sudden death due to CHD; U.S. white males age 30-59 at entry; all rates age-adjusted by 10-year age groups to the U.S. white male population, 1960 (6, 6a-k).

Figure 2: Effects of diet saturated fat, polyunsaturated fat, cholesterol and plant sterols on serum sterols and triglycerides. O'Brien et al., J. Nutr., in press.



UNIVERSITY OF SOUTHERN CALIFORNIA,
DEPARTMENT OF MEDICINE,
Los Angeles, Calif., May 23, 1977.

Senator GEORGE MCGOVERN,

U.S. Senate, Select Committee on Nutrition and Human Needs, Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you for your letter and for the copy of Dietary Goals for the United States published by the United States Senate Select Committee on Nutrition and Human Needs.

I agree with the goals for dietary change as stated and believe that these will reduce the average blood cholesterol and blood pressure level of Americans. This in turn should reduce the incidence of premature coronary heart disease, which is now a major cause of morbidity and mortality among Americans in their most productive years. In addition to the evidence cited in the Dietary Goals for the United States that lower blood lipid levels will reduce premature cardiovascular mortality, I can cite recent, direct experimental evidence which is correlative. We have found that in patients with elevated blood cholesterol and triglyceride levels, reduction of these levels is associated with a favorable change in blood vessel walls. Atherosclerotic lesions become smaller when blood lipid levels are lower. I am enclosing with this letter a recent publication which presents details of the evidence.

I note that the Committee's recommendations begin with a program in public education on nutrition. I subscribe to this goal also, but must point to an important omission. I find no provision in the recommendations for nutrition instruction to those in greatest immediate need of it—those who have been recognized to have elevated blood lipids and blood pressure. These individuals need specific instruction on how to modify what they now eat to a more healthful diet. I have been actively engaged in study of nutritional problems in such patients for 25 years. My experience leads me to believe that there is no substitute for diet teaching by qualified health personnel who can ascertain what the patient eats and make specific recommendations for diet change.

The health delivery system in the United States is not adequately structured to teach patients at high risk of cardiovascular disease what they should eat. In part this is because most doctors receive inadequate instruction in the area and very few other qualified personnel are available to give it. There is little incentive to increase the number of trained personnel because the current system to pay for health care has no realistic provision to support those who offer instruction.

An editorial which appeared in the JAMA, Nov. 29, 1976, page 2534, presents results of a survey of medical school curricula regarding nutrition instruction. This survey indicated that only 17 percent of schools included such instruction in their curriculum. In addition, only seven percent included sufficiently detailed instruction to allow calculation of nutrition in quantitative terms.

In the State of California in 1974, a survey was conducted among members of the California Dietetic Association to learn how many offered therapeutic nutrition instruction in private practice. The number was found to be 42 in a state where 21.1 million people reside.

Taken together, all of this indicates that an average American who learns of a personal problem with elevated blood lipids or blood pres-

sure and who wishes to change to a more healthful diet cannot gain access to qualified instruction. This occurs because qualified personnel are too few in number and because there is no provision in the usual payment plans for health care to allow therapeutic diet instruction.

I hope this information will be helpful to your Committee.

Best wishes.

Sincerely,

DAVID H. BLANKENHORN, M.D.,
Professor of Medicine,
Director-Cardiology.

Enclosure.

Regression and Progression of Early Femoral Atherosclerosis in Treated Hyperlipoproteinemic Patients

ROBERT BARNDT, Jr., M.D.; DAVID H. BLANKENHORN, M.D., F.A.C.P.;

DONALD W. CRAWFORD, M.D.; and SAMUEL H. BROOKS, D.Sc.; Los Angeles, California

Femoral angiograms were done to evaluate change in early atherosclerosis in 12 patients with type IV hyperlipoproteinemia and 13 with type II hyperlipoproteinemia. The patients' average age was 48 years; only one had claudication. Elevated blood lipids and blood pressure were treated with drugs and diet. Repeat angiograms after an interval of 13 months showed regression of atherosclerosis in nine patients, no change in three, and progression in 13. Comparison of preangiogram levels with average levels between angiograms showed significant reduction in serum cholesterol, triglyceride, and blood pressure in the group with lesion improvement but not in the group with lesion progression. Sporadic examples of human atherosclerosis regression are known, but most other studies in man indicate only atherosclerosis progression. Our different result appears due to our selection of patients and radiographic method. We have studied patients with earlier atherosclerosis than previous workers, using a radiographic procedure more sensitive to small changes in lesions.

EXPERIMENTS with hyperlipoproteinemic animals indicate that established atherosclerotic lesions can show regression in swine treated with diet and clofibrate (1), Rhesus monkeys treated with cholestyramine (2), and pigeons treated with partial ileal bypass (3). Information regarding atherosclerosis regression in treated hyperlipoproteinemic humans is more limited. The most encouraging report to date is of 22 patients treated by surgical partial ileal bypass to produce a 40% lowering of serum cholesterol (4). Repeat coronary angiography after an average interval of 3.6 years showed evidence of lesion regression in three patients. In 12 patients, coronary lesions showed no change; in five, significant progression; and in two, equivocal change. Pelvic atherosclerosis showed no change in nine of these patients restudied after 4 to 7 years. In another study of lipid lowering by ileal bypass, coronary angiographic evidence of progression was seen in five of six patients after an average interval of 25 months (5). Ileal bypass had reduced serum cholesterol 48% and serum triglyceride, 41%. A 1-year study of medical therapy by Cohn, Sakai, and Langston (6) randomly assigned 40 patients with

minimal hyperlipoproteinemia to clofibrate or placebo. Significant lowering of triglyceride level was produced by clofibrate but not by placebo treatment. Similar rates of atherosclerosis progression were seen with both therapies, and no patient showed lesion regression.

We have developed two methods for atheroma assessment in femoral angiograms that appear specific and capable of detecting relatively early atheromas. One is an instrumental method using computer controlled image dissection (7, 8). The other uses human film readers but entails modification of visual film-reading procedure to enhance objectivity and reproducibility. Using the visual method we have found that moderately severe, but non-obstructive, femoral atherosclerosis occurs with high prevalence in young hyperlipoproteinemic patients without symptoms of peripheral vascular disease (9). We now report results of repeat study in 25 of these patients after an interval of therapy averaging 13 months. Changes have been detected by both instrumental computer image dissection method and visual film reading. Results by both methods indicate that human atherosclerosis regression can occur more frequently than indicated in previous reports. In this report, we describe atherosclerosis change detected by the visual reading method and correlation of this change with clinical data.

Patients and Patient Management

Twenty-five outpatients, 22 to 65 years of age, referred to the Los Angeles County-University of Southern California Medical Center's Cardiac Lipid Clinic were studied. The most common cause for referral to our clinic was inadequate lowering of blood lipid levels with drug therapy or difficulty in compliance to diet. Sixteen patients were asymptomatic, nine had a history of previous myocardial infarction or angina pectoris, but only one had claudication. Twelve patients had type IV hyperlipoproteinemia, and 13 had type II hyperlipoproteinemia as determined by total serum cholesterol (10), triglyceride (10), and lipoprotein electrophoresis on cellulose acetate (11). All patients were euthyroid with normal liver function. Patients were seen at monthly intervals by a physician and nutritionist. Sitting blood pressure and smoking habits were recorded. Fasting blood lipid levels and uric acid values were ascertained monthly. Intravenous glucose tolerance testing was done by the method of Wahlberg (12) during hospitalization before each angiogram. These data are presented in Table 1.

The National Heart and Lung Institute's hyperlipoproteinemic type specific diet therapy was prescribed and diet compliance estimated. Diets were modified to reduce sodium intake to 1 g/day if diastolic blood pressure exceeded 90 mm Hg. Weight

► From the University of Southern California School of Medicine and the Los Angeles County-University of Southern California Medical Center, Los Angeles, California.

Table 1. Clinical Characteristics of Patients*

Patient	Age	Sex	Race	Percent of Ideal Body Weight†	Cholesterol‡	Triglyceride‡	Glucose K§	Uric Acid‡	Blood Pressure	
									Systolic	Diastolic
	yrs				mg/dl	mg/dl	ml/min	mg/dl	mm Hg	mm Hg
Progression										
1	50	M	B	102	277	109	2.10	5.6	153	100
2	56	F	O	95	351	63	1.19	4.3	117	65
3	37	M	W	135	343	1189	1.16	8.3	144	85
4	39	M	B	99	323	60	1.11	4.8	119	80
5	29	M	W	107	260	171	1.28	7.1	140	88
6	39	M	M-A	130	309	1444	0.42	4.4	133	83
7	54	F	M-A	182	285	227	0.22	6.8	151	100
8	48	M	W	98	463	349	1.75	6.4	114	76
9	49	F	M-A	118	289	616	0.66	6.0	117	78
10	38	M	M-A	95	252	240	1.10	7.3	133	83
11	32	M	W	139	454	2756	0.87	5.5	117	81
12	47	M	W	103	217	168	0.90	7.8	122	73
13	52	M	M-A	147	284	386	0.74	7.8	131	89
No change										
14	62	F	W	134	214	198	1.24	4.7	119	78
15	22	M	O	88	293	76	0.96	4.9	114	72
16	65	M	W	92	325	124	0.79	5.3	118	66
Regression										
17	38	M	W	105	216	71	1.20	5.9	121	80
18	50	M	W	108	272	152	0.82	7.8	121	78
19	36	M	W	106	209	109	1.43	5.5	120	78
20	48	M	W	113	282	128	0.68	6.7	115	74
21	48	M	W	119	257	145	0.96	6.5	123	82
22	50	M	W	122	243	208	0.82	6.3	138	80
23	36	M	W	104	196	83	1.65	4.7	105	67
24	62	F	B	139	267	89	1.19	5.8	128	86
25	50	F	W	104	270	298	1.13	7.6	134	87

* B = black; O = Oriental; W = white; M-A = Mexican-American; By = saphenous vein coronary bypass; V = Vinegar procedure; A = ventricular aneurysm resection; U = unknown; F = familial hyperlipoproteinemia (see kindred data); N = nonfamilial; E = significant ethanol intake (patient is working regularly); D = diabetes mellitus requiring insulin therapy; C = chronic ethanolism (patient is unable to work).

† Statistical Bulletin 40(3), Nov-Dec 1959, Metropolitan Life Insurance Company.

‡ Determined monthly; average value between first angiogram and second angiogram.

§ Glucose disappearance rate, 25-g intravenous glucose tolerance (12). Average of two determinations, one before each angiogram.

|| Determined monthly; average value between first angiogram and second angiogram.

** Cigarettes per day; average between first angiogram and second angiogram.

†† Number of affected persons, number tested.

loss was prescribed for patients above ideal body weight. Eight type IV patients were treated with clofibrate. Additional therapy to reduce lipid level in clofibrate-treated patients included neomycin sulfate for clofibrate-associated increase in low density lipoprotein (13), one patient; and insulin for adult onset diabetes, one patient. Four type IV patients were treated with ticaric acid. Seven type II patients were treated with clofibrate plus neomycin sulfate and six with clofibrate alone. Prescribed drug dosage in all patients included clofibrate, 2 g/day; neomycin sulfate, 2 g/day; and ticaric acid, 1 g/day. Blood pressure lowering agents were hydrochlorothiazide, eight patients; hydrochlorothiazide plus methyldopa, one patient; and reserpine, one patient. In all patients, therapy had been started before the first angiogram and was continued without change until the next angiogram.

Clinical Radiographic Technique

The average interval between angiograms was 13 months. Patients were admitted to the USC Clinical Research Center and taken off all medication except insulin at 72 h before angiography. Written informed consent was obtained by a protocol approved by the USC Research Committee.

Fifty milligrams of diphenhydramine hydrochloride and 30 mg of pentazocine hydrochloride were given intramuscularly 20 minutes before the procedure. Brachial blood pressure and pulse were recorded before and after sedation. Atropine sulfate, 0.4 mg, was given intramuscularly if the pulse was less than 65 beats/min.

Patients were positioned supine on the X-ray table with thigh and leg straight and lower film edge at the superior aspect of the patella. The foot was stabilized by soft restraints to an angle of 45° external rotation. The center of the X-ray field was marked on the thigh, and measurements from this point to the superior patella edge, the X-ray table, and around the circumference of the leg were recorded for later use to position and radiograph each patient identically during a second angiogram. High contrast films, Kodak RP X-omat[®], were exposed with a film changer using a stationary grid, a par speed screen, and a constant potential generator. Scout films taken with exposure factors chosen by thigh size were measured with a 1-mm focal spot densitometer† and background density adjacent to the artery selected to maintain all expected contrast densities within the linear portion of the film recording range. Background densities of second angiograms were matched to those of the first by adjusting scout film kilovolts, peak, while maintaining constant milliamperes and exposure time. Exposure factors ranged from 64 to 80 kV, peak, 100 mA for 0.05 to 0.08 seconds. Focal spot size was 1.0 mm. An average thigh received 67 kV, peak, 100 mA for 0.08 seconds. The X-ray source to film distance was maintained constant at 40 inches and equal magnification during each examination shown by caliper measurement of bone width.

An 18-gauge needle was inserted into the femoral artery after

* Kodak RP X-omat, Eastman Kodak Co.; Rochester, New York.

† Matherly TD504, Royce Photographics Supply Inc.; Glendale, California.

Table 1. (Continued)

Smoking Level**	Previous Myocardial Infarction	Angina Pectoris	Previous Cardiac Surgery	Claudication	Phenotype	Familial Status	Kindred Data††	Secondary Factors	Tendon Xanthomas
0	+	+	0	+	II	U	0/0	0	0
0	0	+	0	0	II	F	7/7	0	+
40	0	0	0	0	IV	U	0/0	E	0
25	0	0	0	0	II	U	0/0	0	0
40	0	0	0	0	II	F	2/2	E	0
10	0	+	0	0	IV	U	0/0	0	0
0	0	0	0	0	IV	U	0/0	D	0
0	0	+	0	0	II	F	2/2	C	+
0	0	0	0	0	IV	U	0/0	0	0
0	0	0	0	0	IV	N	1/3	E	0
0	0	0	0	0	IV	U	0/0	0	0
0	+	0	0	0	IV	U	0/0	0	0
0	0	+	0	0	IV	U	0/0	0	0
0	0	0	0	0	IV	N	1/2	0	0
20	0	0	0	0	II	F	7/7	0	+
0	0	+	0	0	II	F	2/3	0	+
0	0	0	0	0	II	F	2/2	0	0
0	0	0	By	0	IV	U	0/0	E	0
20	0	0	0	0	II	F	2/3	0	0
0	0	0	0	0	II	F	4/5	0	+
0	0	0	0	0	II	U	0/0	0	0
30	+	+	V	0	IV	F	2/2	0	0
0	+	0	By, A	0	II	F	4/5	0	+
10	0	0	0	0	II	U	0/0	0	0
0	0	0	0	0	IV	U	0/0	0	0

lidocaine infiltration and positioned to obtain blood easily by aspiration. A 20-ml syringe containing 60% diatrizoate meglumine was connected to the needle by a short connecting tube containing 1.5 ml of 1% lidocaine. One film was exposed, and the lidocaine-diatrizoate meglumine bolus was injected by hand in 2 to 3 seconds. Four films were taken during the first second after contrast injection, followed by 15 to 18 films taken two per second.

Angiograms were inspected for adequacy of contrast mixing and comparability with previous films before terminating the procedure. Branch angles were examined to confirm replication of leg position on first- and second-year films. All films were adequate for grading with one injection of contrast medium and exceeded the 4.3 ml/sec of 35% iodine-containing medium found diagnostic by Lindbom (14). Film density of background tissue varied from 1.6 to 2.0 optical density. The ratio of vessel contrast media density to background density was calculated as follows: background optical density minus vessel optical density divided by background optical density. This ratio varied from 0.4 to 0.7.

Intraarterial pressure was measured before and 5 minutes after contrast injection with a standard calibrated pressure gauge using a physiologic recorder. An electrocardiogram was recorded continuously from the start of the procedure until 5 minutes after injection. A radiation exposure detector* in the field recorded film exposure times on the electrocardiogram. There were no complications from the procedure, no significant changes in arterial pressure or heart rate. Patients were kept at bed rest for 8 h, and peripheral pulses were evaluated during the 24 h after study.

Film Selection, Randomization, and Grading

Late diastolic films were selected to meet three criteria:

* Nosivol Specialty Co.; Temple City, California.

complete filling of the area of interest with contrast media, which was from at least 15 cm above Hunter's canal to the popliteal space; luminal contours unchanged on three consecutive films; and no evidence of flow separation. A film from the first angiogram was paired with a film from the second angiogram, after which both films were coded and mounted in random sequence. Observers knew that each film in a pair was from a separate examination of the same patient, but they did not know the patient's identity or which film was from the first examination. A modification of the angiographic atheroma assessment method of Dejdar was used. Dejdar and colleagues (15) showed that vessel edge roughness and localized areas of taper correlate highly with gross and microscopic vessel pathology. Our studies of atherosclerosis assessment with a computer controlled image dissector (7, 8) have shown that algorithms that assess vessel edge roughness and major edge indentation significantly predict postmortem vessel morphology and cholesterol content.

Our experience with instrument film assessment led to two new procedures for visual film evaluation that were used in this experiment.

1. We used density-matched, smooth vessel images as comparison standards for detecting small degrees of vessel edge roughness. Comparison images were radiographs of polyurethane blocks filled with a standard 8-mm smooth column of diatrizoate meglumine in varying dilutions (10%, 20%, 30%, 40%, 50%, 60%). Blocks were radiographed in 11 cm of water with a 1-mm focal spot, 4 mA, at 60 to 90 kV, peak. Film graders selected a smooth tube image with contrast density most closely matching the angiogram pair under scrutiny. The smooth tube image was positioned immediately beside vessel segment to be evaluated and used as a reference.

2. We used a segment of normal vessel as a reference for detecting change in vessel lumen by a comparison procedure

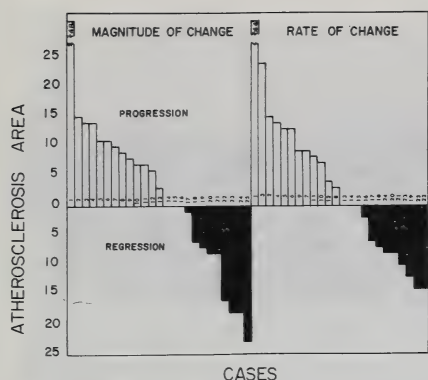


Figure 1. Magnitude, direction, and rate of change in femoral atherosclerosis. Each patient is represented by a bar. Patients showing progression are illustrated by open bars and patients showing regression by solid bars. The magnitude of observed change is graphed on the left; the rate of change per month is graphed on the right. Bar number corresponds to patient identification numbers in Table 1.

using a vernier caliper*, as discussed later. The widest portion of the smoothest proximal segment in each vessel pair was designated "normal reference vessel." The superficial femoral artery has few branches and normally has no significant change in diameter from origin to popliteal artery. Femoral atherosclerosis development is known to begin in Hunter's canal and extend proximally (14-16).

These two procedures were embodied in a measure of deviation from normal vessel width due to atherosclerosis intrusion designated as atherosclerosis area.

The three film graders selected were shown by visual test to recognize 100- μ m pattern variations at film reading distances between 20 and 40 inches. Graders met and agreed on segments to be graded and the location of the "normal reference segment" in each film pair. All other aspects of film reading were done independently. Each grader set a vernier caliper to the width of the "normal reference segment" for that film pair. The preset calipers were next used to compare all segments against the reference segment. The density-matched smooth reference image was used to assess fine edge irregularity. Both edges of a vessel were considered separately, and difference in each segment from reference segment was estimated as a percent of atherosclerosis area. Atherosclerosis area for both edges of a segment were summed and subtracted from the value of the corresponding sum in the other film. These differences in segment pairs were averaged and the film code broken to determine whether such differences indicated atherosclerosis progression or regression. The correlation coefficients between graders were 0.90, 0.91, and 0.83. Atherosclerosis area change by the three graders were averaged, converted to rate of change per year, and used as the dependent variable in further analyses.

The radiographic reading method used in this experiment was evaluated in a separate set of films derived from an autopsy study (7). Radiopaque silicone rubber casts were made at 100-mm Hg pressure in the femoral artery of 26 cadavers and the legs radiographed. Vessels were next removed, opened, photographed in color, and analyzed for total arterial wall cholesterol

content. Gross pathology of arterial segments was ranked according to criteria of the International Atherosclerosis Grading Project. Details of the procedures used have been described elsewhere (17). The correlation of estimates of atherosclerosis area by visual assessment of cast rank, with gross pathology estimate of specimen rank, was $R = 0.86$, $P < 0.001$. Correlation of atherosclerosis area with cholesterol content of arterial wall was $R = 0.80$, $P < 0.001$.

The radiographic reading method used in this experiment was also evaluated by duplicate reading of clinical angiograms by the computer controlled image dissector method developed in this laboratory (7). The correlation of visual reading with a computer controlled image dissector atheroma index was $R = 0.68$, $P < 0.001$.

Results

Figure 1 illustrates the magnitude, direction, and rate of change observed in femoral atherosclerosis. Both the magnitude and rate of change appear to be a continuum, with progression gradually merging into no change and regression. Thirteen patients showed change in the direction of progression; three patients showed no change. Nine patients showed regression. The rate of change in patients showing progression was slightly greater than those showing regression, but this difference is not significant. Clinical characteristics of patients in the three groups are shown in Table 1.

Figures 2 and 3 illustrate an example of regression of atherosclerosis in a type II patient angiogrammed at an interval of 22 months. This is Patient 23 in Table 1.

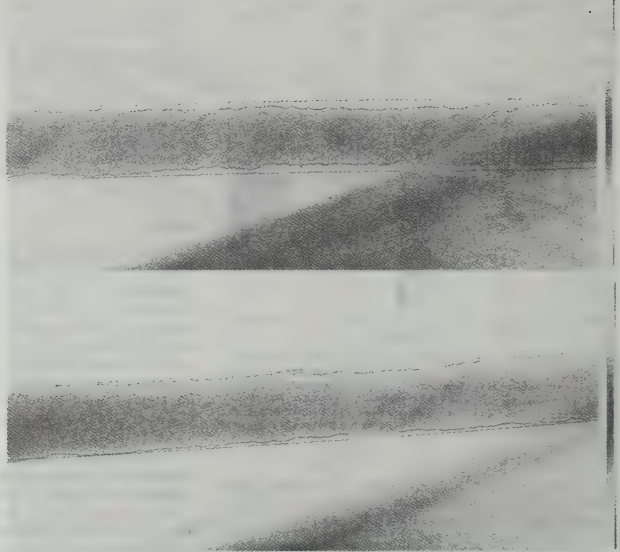
The data in Table 2 demonstrate that patients in the group showing regression had change in serum cholesterol level significant at the 0.1% level when the average of all cholesterol values between angiograms was compared with an average obtained upon entry into the clinic. Compared in an identical manner, patients in the group showing progression of atherosclerosis had no significant change in average serum cholesterol levels. Patients showing regression also had changes in serum triglyceride level and systolic and diastolic blood pressure significant at the 5% level, but those in the group showing progression did not. Glucose tolerance did not change significantly in either group.

Before the first angiogram, risk factors shown in Table 3 did not significantly differ in the group showing regression and progression. In the interval between angiograms, average cholesterol level of the group showing regression was significantly lower than that of the group showing progression, $P < 0.05$ (Table 3). Other risk factors did not differ significantly between the two groups.

In addition to group comparisons, a patient-by-patient analysis of risk factors in the interval between angiograms was done by multiple linear regression. The independent variable was atherosclerosis change per month, and cases were weighted according to square of the interval between angiograms. Independent variables were age, sex, relative weight, serum cholesterol level, serum triglyceride level, systolic blood pressure, uric acid, smoking, and glucose disappearance rate. Systolic blood pressure was significant ($P < 0.01$), other variables were not. An identical result was obtained by this analysis when cases were weighted according to interval between angiograms.

* Mitutoyo, Model No. 532-119; 6-inch accuracy ± 0.01 mm. U.S. Bureau of Standards.

Figure 2. Enlarged segments of femoral angiograms from a xanthomatous type II patient. The vessel is shown before it crosses the femur in Hunter's canal. The film on the bottom was obtained 22 months after the film on the top. Vessel edges and reference edges have been plotted by computer (7), with reference edges equally separated in both films.



Discussion

Regression of femoral atherosclerosis has been observed in nine of 25 treated hyperlipoproteinemic patients examined by angiography at an interval of 13 months. Both type II and type IV patients have shown atherosclerosis regression. These are the first hyperlipoproteinemic patients showing evidence of atherosclerosis regression except for three patients previously reported by Knight and co-workers (4).

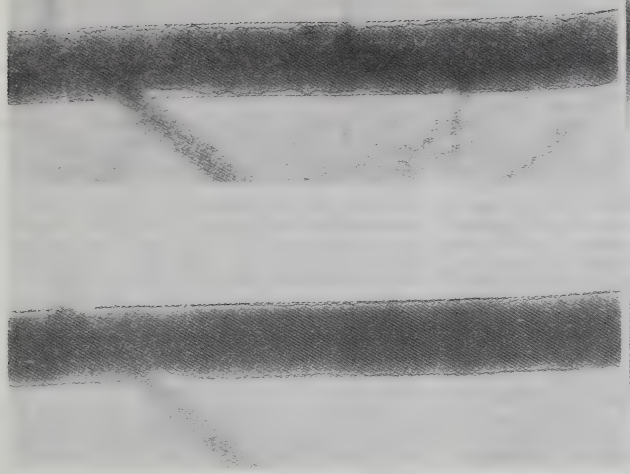
Patients with plaque regression in this study had significantly lower serum cholesterol levels than those showing progression. It is noteworthy that lipid lowering in all of our patients was less and the interval between X rays shorter than in previous studies where comparable patients showed no atherosclerosis regression (5) or only infrequent evidence of regression (4). It seems probable that we have observed more frequent and rapid lesion regression because we have studied earlier, smaller atherosclerotic lesions than previous workers. Cholesterol turnover in human atherosclerosis has been demonstrated with radioactive sterol and is more rapid in superficial portions of the lesions (18, 19). If serum lipid lowering alters plaque lipid influx rate, early plaques, which are thin, should show the most rapid change.

We believe we have observed earlier atherosclerosis than have previous studies because we did angiography of the femoral artery in young persons with few symptoms of peripheral arterial insufficiency. For example, our patients

had much earlier atherosclerosis than those treated intermittently with low fat diet by Coran and Warren (20), who selected patients for study because of claudication and a clinical diagnosis of arteriosclerosis obliterans. Coran and Warren's patients all showed an "inexorable progression" of lesions, but every patient had at least one stenosis occluding 90% of the lumen at onset of the study. None of our patients had lesions this severe at onset of our study, although one had claudication. Similarly, comparison of cases reported by Chilvers, Thomas, and Browse (21), Kuthan and associates (22), and Warren and associates (23) to evaluate the natural history of atherosclerosis obliterans indicates that our patients had atherosclerosis at much earlier stages of development.

Technical factors involved in angiography have allowed us to evaluate earlier lesions than have previous studies of patients treated with surgical ileal bypass or clofibrate. Compared with coronary or pelvic arteries that have been angiogrammed previously to evaluate lipid lowering by surgery or drugs, the superficial femoral artery is straight, unbranched, and motion-free. In addition, the femoral artery is surrounded by thinner structures with more homogeneous X-ray absorption. These anatomic features plus physical principal of X-ray dictate that smaller lesions can be resolved in femoral artery than in pelvic or coronary vessels. To study the femoral artery, we developed an angiographic procedure designed to evaluate lesion change, with specific emphasis on wall details in short

Figure 3. Enlarged segments of femoral angiograms. Midhigh views from the patient shown in Figure 2. The film on the bottom was obtained 22 months after the film on the top.



segments of arteries. We positioned patients, exposed radiographs, and injected contrast media on first examination with the specific goal of obtaining a duplicate angiogram later. Our procedure differs from the usual practice of pelvic or femoral angiography, which outlines a large vascular bed at one examination to provide information about obstruction and collateral flow. High quality angiograms taken to meet usual clinical goals are difficult to compare with a second similar examination because of cumulative differences in detail. Knight and co-workers (4) were able to find only 30 comparable film pairs after performing serial arteriography to evaluate ileal bypass in 120 patients. Chilvers, Thomas, and Browse (21) reviewed 5 years' clinical experience with translumbar aortography and found 75 patients with two or more examinations; eight had comparable femoral artery film pairs. We have found that to measure atherosclerosis change, the first angiogram must be done with the specific goal of achieving comparability with a second later angiogram. We are able to achieve this goal in all patients.

Blood lipid and blood pressure levels were the two risk factors most predominantly associated with atherosclerosis change in our study. Reduction of both was associated with atherosclerosis regression. To analyze the effect of risk factor change in a manner comparable to that used in animal experiments of atherosclerosis regression, risk factors should be known during a "control" period when atherosclerosis develops. The majority of our patients had

been treated by others before entering our clinic, and we reduced blood lipid levels further by additional therapy, or more rigorous diet, or both. We do not have complete data for previous risk reduction therapy in our patients or long-term data on risk factor levels. Data in Table 3 for the period before our first angiogram were obtained in our clinic during a period not less than 3 months. These are the best available estimates of risk factors during a "control atherosclerosis development" period. Using these estimates, patients with atherosclerosis regression showed a significant decline in serum cholesterol ($P < 0.01$), triglyceride ($P < 0.05$), and blood pressure ($P < 0.05$) from levels before the first angiogram to levels between angiograms. This was not seen in patients showing atherosclerosis progression.

Levels of both triglyceride and cholesterol were high and variable before the first angiogram but not significantly different in the two groups later showing regression or progression. In the interval between angiograms, cholesterol level was significantly lower in the group showing regression than in the group showing progression ($P < 0.05$), and the variability of cholesterol from one patient to the next in the regression group was reduced. Triglyceride level continued to vary greatly from one patient to the next in the period between angiograms in both groups and was not significantly different in the groups showing regression and progression. Systolic blood pressure, which was not unusually high or variable before the first

Table 2. Risk Factor Reduction, Average Values on Entry into the Clinic Compared with Average Values Between Angiograms (Paired *t* Test)

Variable	Regression			Progression		
	Average Reduction	<i>t</i> Value	Significance Level	Average Reduction	<i>t</i> Value	Significance Level
Cholesterol, mg/dl	65.22	7.74	0.001	19.38	0.59	NS*
Triglyceride, mg/dl	219.00	3.00	0.05	121.69	0.56	NS
Systolic blood pressure, mm Hg	9.22	2.54	0.05	8.15	1.44	NS
Diastolic blood pressure, mm Hg	5.56	2.57	0.05	6.08	1.60	NS
Glucose disappearance rate, mg/h	0.28†	1.54	NS	-0.14†	-2.04	NS

* Not significant.

† Reduction in the rate of glucose disappearance was found in the group showing atherosclerosis regression, and an increased rate was found in the group showing progression; neither change was significant.

angiogram or between angiograms, had an interesting effect when the rate of each individual's atherosclerosis change between angiograms was analyzed by multivariate regression. Systolic blood pressure level was significant at the 1% level in this analysis and was the only significant variate. Diastolic level was also significant at the 1% level when substituted for systolic in the same regression analysis.

We interpret our data as indicating that lowering of blood lipid and blood pressure levels to a degree that is followed by regression of early femoral atherosclerosis can be produced by drugs and diet in type II and type IV hyperlipoproteinemia. We believe that the important result of this study is evidence that a total effect of all therapy can influence early atherosclerosis favorably. We do not think that our current results should be interpreted on the relative efficacy of individual drugs or diets or over-interpreted on the relative importance of individual risk factors.

In general, the process of femoral atherosclerosis regression or progression can be considered representative of what pertains in other vascular beds, although regional differences in atherosclerosis exist and can be clearly seen in animal models (24). We believe that our findings on risk factors may be relevant to early coronary atherosclerosis regression and progression in treated hyperlipoproteinemias. However, this hypothesis cannot be tested definitively until coronary lesion diagnosis with the precision and sensitivity of the early femoral lesion diagnosis used in this experiment becomes available.

There are several reasons why results presented here

should not be interpreted too broadly in relation to the general problem of atherosclerosis. First, the number of patients is small, and patients were selected. Second, our estimate of risk factor status during a "control period" of atherosclerosis development is limited. Third, the visual atherosclerosis measurement we have used, although sensitive, is not expressed in quantitative terms relative to the amount of preexisting atherosclerosis. Last, the improvement we have observed is in lesions at an early stage of development. Patients presenting with clinical manifestations of atherosclerosis frequently have more advanced and complex lesions. This study does not indicate whether treatment of hyperlipoproteinemia will improve more advanced arterial lesions in patients with symptomatic vascular disease. Nonetheless, it seems encouraging that early human atherosclerosis associated with hyperlipoproteinemia can show improvement when patients are treated.

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►Requests for reprints should be addressed to Robert Barndt, Jr.,

Table 3. Average Risk Factor Levels Before the First Angiogram and Between Angiograms*

	Cholesterol	Triglyceride	Percent of Ideal Body Weight†	Uric Acid	Glucose K ‡	Blood Pressure		Smoking Levels§
	mg/dl	mg/dl		mg/dl	ml/min	Systolic mm Hg	Diastolic mm Hg	
Before first angiogram								
Regression	311 ± 42	362 ± 279	115 ± 17	6.4 ± 0.9	1.4 ± 0.7	132 ± 15	85 ± 8	8 ± 11
Progression	335 ± 65	720 ± 722	119 ± 26	6.7 ± 1.7	0.9 ± 0.5	138 ± 25	89 ± 17	12 ± 15
Between angiograms								
Regression	246 ± 31	143 ± 72	113 ± 12	6.3 ± 1.0	1.1 ± 0.3	123 ± 10	79 ± 6	7 ± 11
Progression	316 ± 73	598 ± 779	119 ± 26	6.3 ± 1.3	1.0 ± 0.5	130 ± 14	83 ± 10	12 ± 18

* Values given are mean ± standard deviation.

† Statistical Bulletin 40(3), Nov/Dec 1959, Metropolitan Life Insurance Company.

‡ Glucose disappearance rate, 25-g intravenous glucose tolerance (12).

§ Average number of cigarettes consumed by smokers.

|| Significant difference, *P* < 0.01. All other differences in this table are not significant.

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UNIVERSITY HOSPITAL,
THE UNIVERSITY OF MICHIGAN,
Ann Arbor, Mich., May 10, 1977.

Senator GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs, U.S.
Senate, Washington, D.C.*

DEAR SENATOR MCGOVERN: Thank you for your invitation to comment on the booklet prepared by The Select Committee on Nutrition and Human Needs of the United States Senate. I have examined this document carefully and agree with the assessment of the problem of poor nutrition among the American people. I believe the evidence linking nutrition to atherosclerosis is very strong indeed, and this should be emphasized as the primary reason for recommending alterations in the American diet. Evidence that nutrition is as clearly associated with many of the other chronic diseases seems more flimsy and could, in fact, detract from the impact of the report on dietary habits which predispose people to atherosclerosis and hypertension.

The suggested changes in diet are in the right direction, but in my opinion do not go far enough in terms of substituting polyunsaturated fats for saturated and monounsaturated fatty acids. The implication from the report is that any fatty acid that is not fully saturated is beneficial, but monounsaturates are not and should therefore be considered in a different category than the polyunsaturated fatty acids. This, of course, requires more ingenuity and a greater willingness to adapt to a new sort of diet. However, the work of Dr. Ancil Keyes in his studies in seven countries around the world and the studies of Dr. Leren in Oslo, Norway, point quite strongly to the extreme importance of a high proportion of polyunsaturated fats in the diet and a very low proportion of saturated or monounsaturated fats.

Implementation of the program of course will also pose many problems and will be a frustrating experience to say the least. I feel that health education along this line should start in the schools where children and parents can be involved in the educational process. In spite of apathy and indifference among the population and undoubtedly resistance by vested interests in the food industry, such an effort is worthwhile. I am particularly concerned at the present time by the rapid proliferation of the so-called fast food chains which offer inexpensive meals and are very attractive to people who wish to eat out more frequently than in the past. Such establishments invariably use large amounts of saturated fats because of their cheapness and feature many carbonated, sugary drinks and desserts which are high in both sugar and saturated fats. I believe the attraction of such establishments will be very difficult to encounter, but at the same time, people should be well informed about the low quality of the food they are ingesting at such places.

As a matter of personal philosophy, I do not favor any coercive measures which could be enacted by the government at various levels to restrict the use of certain types of food and encourages the use of others. I would much prefer that people made such decisions on their own after appropriate education regarding diet. At the same time, I would think it was entirely appropriate for federal, state and local agencies to monitor any counter claims regarding the healthfulness

of dietary constituents which are clearly undesirable. I think the model for governmental action is that applied to the tobacco industry.

Once again I appreciate the opportunity to comment on your very worthwhile and important endeavor and wish you well in further work along this line. If I can be of any service, please do not hesitate to let me know.

Sincerely yours,

L. D. OSTRANDER, M.D., *Professor.*

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
PUBLIC HEALTH SERVICE,
NATIONAL INSTITUTES OF HEALTH,
Framingham, Mass., May 16, 1977.

HON. GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs,
Washington, D.C.*

DEAR SENATOR MCGOVERN: Thank you for the copy of the Committee Report, "Dietary Goals for the United States". As you have noted, this is a long overdue set of recommendations vital to the health of the United States. The goals stated are widely supported by those interested in the prevention of cardiovascular disease, despite the impression created by a vocal minority which receives too much attention from the press and the medical journals.

This is a good start. Implementing these goals will be even more difficult than obtaining a consensus as to what these goals should be. However, it is an important task which, if successful, could have a substantial effect in reducing the appalling annual toll of preventable cardiovascular mortality.

Sincerely yours,

WILLIAM B. KANNEL, M.D., *Medical Director.*

CANCER CONTROL PROGRAM,
DUKE COMPREHENSIVE CANCER CENTER,
Durham, N.C., May 23, 1977.

HON. GEORGE MCGOVERN,
*U.S. Senate, Select Committee on Nutrition and Human Needs,
Washington, D.C.*

DEAR MR. CHAIRMAN: I was delighted to receive your "Report" enclosed in your letter of May 2, 1977. Two days later I received a second letter, dated May 4, and I am responding to both of these letters. Enclosed you will please find my comments. As you can see, I am in complete agreement with the description on goal 3, 4, 5 and 6. I was amazed at the bold approach to hypertension decreasing the salt consumption to 3 grams per day. For your information, I have enclosed our own experiment, conducted in the community of Evans County, Georgia, reducing the salt intake of hypertensive, obese persons to 3 grams a day for a period of one year. The results were excellent.

My only disagreement is outlined in my comments to goal 1 on the treatment of obesity. A few additional comments were necessary on the association of cancer and fat intake (goal 2).

Generally speaking, I think this report constitutes a major breakthrough, and you and your committee has to be congratulated on the outstanding work done on behalf of and for the people of the United States. My only concern is that not enough publicity has been given to the Senate Report when it was published in February of 1977. After you have received all additional comments which you have requested, you should launch a major press campaign in order to bring the content of the Senate Report to the attention of every American.

If you have any further questions, I will be glad to answer them in person or in writing.

With kind regards.

Sincerely yours,

S. HEYDEN, M.D.

*Professor, Community Health Sciences,
Duke University Medical Center.*

COMMENT ON GOAL I

(With particular reference to p. 25)

While I agree with all that has been said about the treatment of obesity, I take strong issue with the paragraph (p. 25) quoted from Professor O. Mickelsen concerning the use of bread in a weight reduction program. Twelve slices of bread per day would be disastrous even for most normal weight persons. It is a disservice to the American public if this paragraph would be retained in a future edition of the U.S. Senate Report. To be more specific, there are several types of calorically restricted bread on the market, varying from 58 to 64 calories per slice. If regular bread was used in this experiment, we may safely assume that each slice contained at least 100 calories which would mean a caloric intake of 1,200 calories from the bread alone. (Dr. Mickelsen does not state what kind of bread spread was used, adding to the further increase in calories.)

In 1971 and 1973 we published the method and first results from the "Workingman's Diet", and discussed the temporary elimination of bread during the period of active dieting. I consider this a mandatory requirement in weight reduction for several reasons:

(1) The carbohydrates derived from bread as well as from potatoes and from starches in general "shoot" into the blood stream, increasing the blood sugar of most obese persons to an undesirable degree (hyperglycemia). Diabetologists agree that this classical hyperglycemia reaction of obese patients (who are not diabetics) to bread and starches is caused by what the experts call "insulin resistance." This means a delay in the release of insulin from the pancreas, allowing the blood sugar level to augment unchecked until, finally, insulin is secreted in a large amount (hyperinsulinemia). The excess of insulin in the blood leads to a quick decrease of the blood sugar level, followed by what diabetologists have termed hypoglycemia—a blood sugar level which usually is considerably lower than the fasting serum glucose concentration. Hypoglycemia manifests itself with symptoms ranging from extreme fatigue, cluster headaches, irritation and "black out" to hunger. This feeling of hunger has been described in particular by obese patients undergoing a glucose tolerance test during the third

or fourth hour while the blood sugar drops from a high peak level to a very low level. Why, then, should we advise obese patients to eat bread (and lots of it) if we know that they will have to suffer from these biochemical reactions.

(2) Farmers have known for centuries that feeding of cattle and hogs with bread and grain, leads to almost instantaneous conversion of carbohydrates into fat. This observation applies to overweight human beings just as well: If obese, sedentary individuals consume a high carbohydrate diet, this will be deposited as adipose fat tissue, certainly another reason for restricting the carbohydrate intake in the obese to those carbohydrates derived from skim milk products, vegetables and fruits (in that order).

(3) For the past decade several scientists have demonstrated that a high carbohydrate diet will result in the retention of sodium and thus lead to fluid accumulation in the body in contrast to a diet high in protein and/or fat. The difficulty in balancing the salt and fluid intake and output is well recognized, particularly in obese women. Why, then, should we add to the struggle of the obese? There is certainly no need to go into the other extreme, the Atkin's or Stillman's "diet", limiting the carbohydrate intake to 2 percent of the total caloric consumption with the danger of a sharp rise in the cholesterol (and triglyceride) levels in the blood. In summary, we would welcome a revision of the previously mentioned paragraph, if not complete elimination. It should be recognized that prevention and treatment of obesity is one of the major challenges of the next decades. We need to take this problem more serious than could be implied from Dr. Mickelsen's experiment. One can think of many advantages if treatment of obesity were successful, but none would be greater than the resulting benefit for a majority of 25 million Americans suffering from hypertension. We came to this conclusion from a cooperative national hypertension intervention study, of which Evans County, Georgia is one of the study centers, (Principal Investigator: C. G. Hames, M.D.).

In our work with the Hypertension Detection and Follow-Up Program (HDFP), sponsored by the National Heart, Lung and Blood Institute, we are following 10,940 hypertensive patients, aged 30-69 years, since 1973 for a total of five years in 14 communities across the United States. The most significant finding to date (which we presented at the American Heart Association meeting in San Diego, Calif., March 7, 1977) is that some well-known side effects of long-term antihypertensive drug therapy can be limited or even eliminated if patients lose weight while on medication. Thus, hypertensive patients who lost weight did not develop high uric acid levels (hyperuricemia) or high blood sugar levels (hyperglycemia) and also fared better in their blood pressure reduction in comparison to those patients who remained weight stable or gained weight. Since the primary aim of HDFP is to determine the effectiveness of antihypertensive medication, adjunctive diet counseling was offered to the very obese only (≥ 40 percent above their normal weight). In view of the fact that 60 percent of our hypertensive patients are ≥ 20 percent above their normal weight, the finding of the beneficial effect of weight reduction deserves attention for the future management of essential hypertension. In addition, it should be pointed out that the remaining 40 percent of hypertensive patients are by no means normal weight: Only 11 per-

cent were found to be at ideal weight. (This paper, presented by Dr. Heyden, has not been published yet. It was developed in cooperation with Drs. Tyroler, Borhani, Oberman and Hames.)

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[Reprinted from the January 1972 issue of Reader's Digest]

NOW—THE WORKINGMAN'S DIET

(By Siegfried H. Heyden, M.D., Associate Professor, Department of Community Health Sciences, Duke University Medical Center, Durham, N.C. with Stanley L. Englehardt)

One of the heaviest patients I ever treated was a 360-pound man who had to squeeze sideways through my office door and then stand, because no chair in the room would hold him. Yet the story he told is one that I hear repeatedly from people who are only 20 or 30 pounds overweight:

"I don't like the way I look, and I know these extra pounds are unhealthy. I have tried all the diet fads, and they just haven't worked. Is there any diet that can help me get these pounds off and keep them off?"

There is. We call it the "Workingman's Diet" because it's designed to fit the budget, working schedule and eating pleasure of the average man or woman. The diet combines short periods of fasting for weight reduction with a nutritionally sound 700-calorie daily fare for maintenance of the weight loss.

How did my heavy patient do on this diet? With his bulk, it took nine months for him to reduce to a near-normal 180 pounds. Equally important, he has been able to keep his weight at this level through careful calorie control.

Of Fads and Fasts. Overweight is a problem shared in some degree by more than 60 million Americans. Most of them realize that excess pounds are potentially dangerous to their health—and certainly unattractive. They grasp at every new diet fad that comes along, but few achieve effective and long-lasting weight control. Why?

Most of the fad diets aren't designed for prolonged use. The majority are a variation on the theme of high protein intake with few or no carbohydrates, a regimen which sacrifices the balance of fat, protein, carbohydrates, vitamins and minerals essential to good health. Some of these diets rely solely on unlimited quantities of grapefruit and eggs to "melt away" fat—even though there's no scientific evidence that this, or any other combination of foods, will erase fatty tissue.

Lack of variety in the menu is another reason for long-term diet failure. It takes tremendous will power to pick away at a canned diet food or soup meal after meal. And hospital-supervised diets which

have proved so successful aren't practical for the average overweight nine-to-five working person.

It was for such people that I devised the Workingman's Diet. The reason that fasting is recommended—and possible—as part of this diet is that overweight is represented by stored fat. The burning of this fat provides energy while producing weight loss. Moreover, going without food for short periods does not harm the human organism—as has been demonstrated countless times by religious fasts, some of which last weeks.

CALORIES IN FRUITS

Apple—1 medium-----	80	Orange—1 medium-----	65
Applesauce, unsweetened—½ cup--	50	Orange juice, unsweetened—½	
Applesauce, sweetened—½ cup-----	115	cup-----	55
Apricots, canned, unsweetened—		Peaches, canned, unsweetened—½	
½ cup-----	45	cup-----	40
Apricots, canned, sweetened—½		Peaches, canned, sweetened—½	
cup-----	110	cup-----	100
Apricots, fresh—3 medium-----	55	Peaches, fresh—1 medium-----	40
Apricots, dried, unsweetened—½		Pears, canned, unsweetened—½	
cup-----	120	cup-----	40
Banana—1 medium-----	100	Pears, canned, sweetened—½ cup--	95
Blackberries, fresh—½ cup-----	40	Pears, fresh—1 medium-----	100
Blueberries, fresh—½ cup-----	40	Pineapple, canned, sweetened—	
Cantaloupe—½ (5" dia.)-----	80	large slice-----	80
Cherries, canned, unsweetened—½		Pineapple, fresh—½ cup-----	40
cup-----	50	Pineapple juice, unsweetened—½	
Cherries, canned, sweetened—½		cup-----	70
cup-----	105	Plums, fresh—1 medium-----	30
Cherries, fresh—15 large-----	70	Plums, Italian prune, canned,	
Cranberry sauce, sweetened—½		sweetened—3 medium-----	110
cup-----	200	Prune juice—½ cup-----	100
Dates—3 or 4-----	85	Prunes, stewed, unsweetened—¼	
Figs, dried—1 large-----	60	cup (4)-----	65
Grapefruit—½ small-----	50	Raisins, dry—2 tablespoons-----	50
Grapefruit juice, unsweetened—½		Raspberries, fresh—½ cup-----	35
cup-----	45	Rhubarb, stewed, sweetened—½	
Grape juice—½ cup-----	85	cup-----	190
Grapes—20-----	70	Strawberries, fresh—½ cup-----	30
Honeydew melon—⅓, average		Strawberries, frozen—3 ounces----	90
size-----	60	Tangerine—1 medium-----	40
Lemon juice—3 tablespoons-----	10	Watermelon—1 slice (4" x 8")----	115

Still, most of my patients worry that the fasting, followed by such a small caloric intake—less than one third the normal intake, and about half the amount that the average dieter consumes—will affect their health. Not if the 700 calories provide all the necessary nutrients. On the contrary, the diet has benefited patients with diabetes, gout, hypertension and other cardiovascular problems—all of which diseases have a high incidence among overweight persons. I confirmed this personally years ago, and in research programs during the past five years.

Here is what I discovered myself after World War II, when I was a medical student living in Berlin and rationed to about 700 calories a day. Despite the modest amount of food, the lack of transportation which forced me to bicycle many miles to and from school each day, the physical exertion involved in scrounging for fuel, and the long hours of schoolwork and study, I remained healthy, alert and at a constant weight. The same was true of the people around me. Analysis showed why: the 700 calories represented a nutritious balance of pro-

tein, carbohydrates, vitamins and minerals—with very little fat. I learned that it's not how much but what you eat that plays a vital role in good health.

Ready to Launch. To date, more than 500 overweight people have participated in the Workingman's Diet program under close supervision, and several hundred more have used it on their own. Weekly checkups of each person in the supervised group have shown an average weight loss for women during the first ten weeks of slightly over 30 pounds, and an average weight loss for men of 40 to 50 pounds.

CALORIES IN VEGETABLES

Asparagus, cooked— $\frac{1}{2}$ cup	25	Onions, cooked— $\frac{1}{2}$ cup	30
Beans, green, cooked— $\frac{1}{2}$ cup	15	Onions—6 small green	40
Beets, cooked— $\frac{1}{2}$ cup	25	Parsnips— $\frac{1}{2}$ cup	50
Broccoli, cooked— $\frac{1}{2}$ cup	25	Peppers—1 medium	15
Brussels sprouts, cooked— $\frac{1}{2}$ cup	30	Radishes—4 small	5
Cabbage, cooked— $\frac{1}{2}$ cup	15	Sauerkraut, cooked— $\frac{1}{2}$ cup	20
Cabbage, raw— $\frac{1}{2}$ cup	10	Spinach, cooked— $\frac{1}{2}$ cup	20
Carrot, raw or cooked— $\frac{1}{2}$ cup	20	Squash, summer, cooked— $\frac{1}{2}$ cup	15
Cauliflower, cooked— $\frac{1}{2}$ cup	15	Squash, winter, cooked— $\frac{1}{2}$ cup	45
Celery—3 stalks	10	Tomato, cooked— $\frac{1}{2}$ cup	25
Cucumber—12 slices	10	Tomato, fresh—1 small	20
Eggplant, cooked— $\frac{1}{2}$ cup	20	Turnips, cooked— $\frac{1}{2}$ cup	20
Kale, cooked— $\frac{1}{2}$ cup	20	In case you wish to eat potatoes:	
Lettuce, iceberg— $\frac{1}{2}$ head	35	Baked—1 medium	90
Okra—8 or 9 pods	30	Boiled—1 medium	105

Almost without exception, hypertensive patients—at least one third of all overweight people exhibit signs of hypertension—have brought their blood pressure down to normal, and therefore reduced their chances of suffering a stroke. Likewise, a number of diabetic patients have returned to normal bloodsugar levels, and those with high blood-cholesterol levels are now within accepted bounds. Several patients with gout have been freed from pain—without the use of drugs—since their weight returned to normal.

The Workingman's Diet, it must be stressed, is effective only when taken seriously. It cannot be used piecemeal or only when the spirit moves you. It means a new life-style.

First, have a medical examination that includes a glucose tolerance test, cholesterol and uric acid determination, and a blood-pressure measurement and an electrocardiogram. If your physician gives you clearance for the diet, arrange to provide him with a progress report at least once every two weeks, or as often as he suggests.

Then, invest in the following four items:

1. A reliable scale to weigh yourself each morning.¹ Anything but a loss or maintenance of a loss should be regarded as a signal to lower calorie intake.
2. A scale for precise weighing of meat, fish and cheese.
3. A pocket-size calorie chart to tell you the number of calories in a given weight of food. Guesses usually veer toward the low side.
4. A supply of multi-vitamins, to be taken daily.

¹ See "Your Best Weapon Against Overweight," The Reader's Digest, July '71.

CALORIES IN MEAT AND FISH

The following calorie values for meat and fish are given for three-ounce portions, after roasting, baking or broiling.

Beef:		Veal: Cutlet.....	185
Chuck roast.....	180	Liver: Beef.....	195
Porterhouse steak.....	190	Fish and Seafood:	
Tenderloin	175	Crab meat.....	80
Sirloin Steak.....	185	Lobster, canned.....	80
Tongue	200	Cod	145
Pork:		Halibut	145
Roast	185	Oysters	75
Tenderloin	215	Salmon, pink, canned.....	120
Poultry:		Shrimp, canned.....	100
Chicken, broiled, white meat..	140	Tuna, canned, in oil.....	170
Turkey, roast, white meat.....	150	Tuna, canned, in water.....	110

Now you are ready to launch yourself on the Workingman's Diet. First, face up to the 2½ days of fasting called for each week, usually recommended for Friday afternoon through Sunday night. (During "fasting," an unlimited quantity of non-caloric liquids to replace water loss and to satisfy the psychological need for nourishment is allowed.) Although most dieters discover that they can get through the weekend without trouble—"It gets easier as you go along" is a phrase I've heard many times—some feel hunger pangs strongly on Sunday night. For these people, I suggest "borrowing" Monday's breakfast. Or, they may prefer to go without food every other day, consuming the 700-calorie diet in between. If you can show progress with a shorter fasting period each week—one day, say—then follow that scheme.

Weight losses after the fasts are usually dramatic. While the largest losses generally occur after the first few fasting periods because of the release of fluid from the fat tissue, I've found that each fast accounts for an average loss of two to three pounds per week in women and three to five pounds in men.

The Spice of Variety. There are many ways to divide up the 700-calorie diet that maintains your weight loss. Some like to splurge on a big 250-calorie breakfast, while others never have more than juice (eight ounces of unsweetened orange juice equals 110 calories) and coffee for breakfast anyway and save their calories for lunch and dinner. The Workingman's Diet is not rigid about how the calories should be split up—but we do insist on a reasonable intake of food at least three times a day. Therefore we suggest to all patients that they allocate 140 calories for breakfast, 150 calories for lunch and roughly 400 calories for dinner, and we ask dieters to keep a diary record of their intake.

Here are a few examples of what you can do within these allotments:

Breakfast.—about 140 calories. Choice: one cup of cereal (95 calories) with ½ cup of skim milk (45 calories); or six hard- or soft-boiled egg whites (90 calories) and half a small grapefruit (50 calories); or ½ cup of cottage cheese (about 100 calories) with ½ cup unsweetened peaches or pears (40 calories). Coffee or tea is free (if no calories added).

Lunch.—about 150 calories. Choice: Vegetable-meat soup boiled with water, herbs and dietary salt (the vegetables in the soup equal 100 calories; one ounce of lean meat equals 60 to 70 calories); or two

pieces of fruit (see the fruit calorie chart, page 203); or tossed salad or vegetable platter (see the vegetable calorie chart, page 204). One example: two small carrots, two inner stalks of celery, $\frac{1}{2}$ medium cucumber, two tablespoons of raw onion, one large tomato, $\frac{1}{2}$ head of lettuce. With a dressing of vinegar or lemon juice, this comes to about 150 calories.

Dinner.—about 400 calories. If 300 of the calories are provided by meat or fish (see the meat-and-fish calorie chart, page 205), the remaining 100 calories can be used for vegetables or salad. Especially recommended are sirloin steak, tongue, veal cutlet, chicken and fish.

Of course, all meats and fish should be fat-trimmed and cooked without additional fat. Take advantage, too, of the growing stock of low-sodium and lower-calorie diet foods now available; these mean easy preparation and spelled-out measurements. Don't fail to supplement your diet with daily multi-vitamin capsules.

Alcohol, which has no nutritive value, but is high in calories, should be avoided during this diet. We recommend strongly that the following items also be avoided:

Sodium salt and such products as prepared hams, smoked bacon, tomato juice, mustard, catsup and salad dressings, which contain salt. In addition to being a possible cause of hypertension, salt helps the body to retain fluid, which accounts for many pounds of overweight.

High-calorie vegetables: dried beans, corn, peas.

Sugar. A pure carbohydrate, sugar contains no vitamin or mineral nutrients, but does contain 15 calories per teaspoon—calories which should be allotted to food that provides needed nutrients on a low-calorie diet.

Breads, also carbohydrates.

One of the best times to break the smoking habit is during this diet program. Most overweight smokers complain that they can't stop because it increases their appetite. With the Workingman's Diet, we've found that the reverse takes place. Of more than 100 smokers on our diet program, only 11 failed to break the habit. The likely reason: this diet keeps blood sugar at a balanced level, cutting down hunger pangs.

As a physician, I wish that all those people who are now just "mildly overweight"²—20 or 30 pounds above what they weighed in their early 20s—would get rid of their excess fat before it becomes a serious medical liability.

Experience has shown that it takes about three months for most dieters to get back close to their normal weight. (And, as a general rule, this diet should not be followed for longer than three months.) During this time they must adhere to the fasting 700-calories regimen. The idea is to get as much out of a broad selection of food as possible without exceeding the daily 700 calories.

Once your target weight has been reached, maintenance is up to you. This means using your scales each morning, keeping to a rigid 140 calories for breakfast, 150 calories for lunch, and adjusting your dinner intake to the morning scale reading. Eventually, you will discover the calorie level that is best suited to you—a level that will help you to stay lean and fit for the rest of your days.

² A person's "normal" weight is considered to be, in most cases, what he or she weighed between ages 18 and 25 (assuming the person was not overweight at those ages). Musculoskeletal growth is usually completed by age 25, and any pounds put on thereafter are generally excess fat tissue.

Weight Reduction in Adolescents¹

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Abstract. A weight reduction diet with 700 kcal (90 g protein, 50 g carbohydrates and 15 g fat) and one to two intermittent fasting days per week proved successful for 15 obese, physically inactive adolescents; weight loss averaged 31.4 lb. within 4 months. Intensive dietary instructions of youngsters with their mothers were carried out on an individual basis, with weekly follow-up visits and review of dietary diaries.

Key Words

Protein requirements
Carbohydrate reduction
Intermittent fasting
School performance
Group teaching

In contrast, a group therapy approach toward obesity control in 27 adolescents with the help of former adolescent patients as 'instructors' proved disappointing (average loss of 10 lb. within 2 months). Reasons for a lower success rate were boredom of three long summer vacation months, lack of transportation, frequent disinterest among the families and disruptive family units, ignorance in basic knowledge about nutrition and failure to take advantage of previous experience of other adolescents who had completed their weight reduction.

Introduction

An excellent body of information exists on the etiology of obesity in children and adolescents [1-5] and the physiological consequences of obesity [6, 7], but methods of weight reduction in this age group are mainly limited to increased physical activity programs [8, 9].

In October 1970, a weight reduction program based on caloric restriction and intermittent fasting for obese adolescents was developed after a 2-year experience in obesity control of adults [10]. The program consisted of a

¹ This study was supported in part by a grant from the Research Council of Duke University, Durham, N. C.

700-kcal diet providing an intake of 90 g of protein (emphasizing fish, chicken, egg whites, skim milk, cottage cheese), sodium restriction, less than 3 g per day; substitution through herbs and spices, and, dependant on the degree of obesity, intermittent fasting between 1 and 2 days per week.

The first period with individual patient-doctor contact (including mothers), involving eight adolescents, lasted from October 1970 through May 1971. It was hoped to create community talents among those young adolescents who had successfully undergone weight reduction in order to help others of the same peer group. A group therapy program was conceived as school holiday activity between June and August 1971. The last part of this report covers the time between September 1971 and March 1972, with a return to the individual patient-doctor contact.

Method

Subjects. A total of 51 children and adolescents, ranging in age from 13 to 17 years, with five exceptions – aged 9–12 – were seen at the Obesity Clinic established at the Department of Community Health Sciences of Duke University Medical Center and expressed interest to learn new dietary habits. In the first phase, we started with four white and four black adolescents on an experimental basis in order to test the hypothesis that the method of weight reduction which had proven successful in several hundreds of adults was applicable to young persons. Four of them (two black females aged 15, one white male aged 17 and one white female aged 16), who were especially motivated towards normalization of their weight and who seemed to have the qualities for influencing others of their respective peer group, were then asked to work with us during their vacation months with the promise of a minor financial reward.

Each 'instructor', as we called them, helped with recruiting between six and ten youngsters with obvious overweight. The investigators attempted to develop a group therapy learning experience for grossly overweight adolescents with weekly meetings, lectures, multiple choice tests, games and encouragement for physical activity. All children underwent a physical examination by one of us (W.D.M.). Although this program was under constant medical supervision, the two physicians tried to remain in the background.

Unfortunately, one of the two black girls fulfilled only the first requirement by bringing eight black obese girls into the program but turned out to be a failure in the follow-up. She not only failed to continue her much needed weight loss, but regained 25 lb. rather quickly. Therefore, the eight black girls in this particular group were at a definite disadvantage as they had no leader and no proper follow-up at the time they needed dietary and moral support most. Other contributing reasons for failure were lack of transportation to and from our meeting place, complete absence of interest and motivation as far as the families were concerned, disruptive family units and ignorance in the most basic knowledge about nutrition. Most of these persons (a group of eight obese girls, their instructor and her brother) were seen only once or twice and, therefore, we excluded these children from our analysis.

The report comprises 42 youngsters who were properly informed, either individually or in a group, about the method, had some means of transportation and had the advantage of the availability of an instructor whom they could contact personally or by telephone anytime they wished.

Procedure. Each subject was required to familiarize himself with the calories in the foods permitted for a 700-kcal diet. These calorie lists were simplified, giving in alphabetical order the calories on one page for fish and meat and on one page each for vegetables and for fruits. Visible fat was excluded; thus, the total fat intake was from invisible fat only, roughly 15 g/day (135 kcal). The carbohydrate intake was limited to salads, vegetables and fruits; bread and other baked products as well as sweetened and whole milk dairy products were not permitted with this diet. Therefore, the total intake of carbohydrates amounted to 200 kcal. Protein consumption was forced to 90 g/day (360 kcal).

In view of a calorically deficient diet, the minimum requirements for vitamins, calcium and iron had to be met by substitution from multiple vitamin-mineral capsules, but our main concern was the protein intake. According to the 1968 revised recommended daily dietary allowances by the National Research Council [11], the minimum protein requirement per day for males age 10–12 is 45 g, increasing among 12- to 14-year-old boys to 50 g and at age 14–18 to 60 g. Among 10- to 14-year-old girls, the minimum daily requirement is 50 g protein, increasing at age 14–18 to 55 g. However, according to a more recent study [12], it has been proposed that the recommended allowances for protein for pre-adolescent children be increased to 60 g/day. Adoption of the proposed 60-gram protein intake for pre-adolescent children would raise the level to that of adults.

By requiring each child and adolescent to keep a daily diary of the food intake, it was possible to monitor the protein intake. With only one cup of Special K and $\frac{1}{2}$ cup of skim milk for breakfast, a tuna fish salad for lunch and 6 oz. of chicken for dinner, the 90-gram goal of protein intake was easily reached. Similarly, a breakfast consisting of ten hard boiled or soft boiled egg whites, a lunch consisting of salad mixed with skim milk cottage cheese and a dinner of 9–12 oz. of fish not only provided a protein intake far above the minimum requirement, but at the same time assured a low-caloric intake (of less than 700 kcal) and still proved to be satisfactory. Others preferred, for their breakfast, skim milk yogurt or skim milk cottage cheese mixed with unsweetened fruits, mushroom omelets (made of egg whites) for lunch and turkey for dinner.

Whereas the five younger children were required to abstain from one or two dinners per week, the adolescents in our study group were asked to fast for 1 or 2 days each week with an *ad libitum* intake of non-caloric so-called dietary soft drinks.

Skinfold and height-weight relation measurements were not carried out since all of our children were grossly obese, the boys with obvious accumulation of fat in their breasts, giving the appearance of 'gynecomasty' and the girls with protruding abdomens. The initial weights are given in tables I–III.

Results

Of the eight children who started their weight reduction prior to the group therapy effort, one black girl lost 72 lb. in 5 months, another black girl lost 47 lb. in 4 months, a third black girl lost 74 lb. in 9 months, a white

boy lost 60 lb. in 3 months, one white girl lost 31 lb. in 4 months, a second white girl lost 10 lb. in 8 months (but grew 2 inches during the same time) and a third white girl lost 28 lb. in 6 months. Only one black girl (mentioned previously) was a complete failure by reducing first 25 lb. and gaining it all back within 3 months. Thus, the individual teaching and weekly follow-up by one of us (S.H.) provided an almost 100-percent success rate in weight reduction (table I) with an average weight loss of 40.2 lb. in approximately 7 months.

At the beginning of the summer vacation, a group of 36 adolescents was enrolled in our group therapy program. However, for reasons stated, eight black girls as well as the brother of the instructor were excluded from our evaluation. The analysis of the remaining 27 adolescents is given in table IIa.

In spite of well-planned group sessions, it soon became obvious that the individual patient-doctor program was far more successful. The weekly meetings started with weighing and publicly announcing the loss, gain or standstill acquired during the preceding week. This was followed by a lecture by one of the two participating physicians emphasizing the protein requirement in young adolescents and the consequences of untreated obesity. Examples of particularly well-kept diaries were read in public, and in less perfect diaries, ways of improvement were discussed and new recipes ex-

Table I. Results of individual weight reduction program with intensive dietary counselling and weekly follow-up visits

Race	Sex	Age years	Weight initial, lb.	loss.	
				lb.	months
B	F	15	241	72	5
B	F	15 ¹	241	47	4
B	F	14 ²	220	74	9
B	F	15 ¹	237	0 ³	6
W	F	11	145	10	8
W	F	13	168	28	6
W	F	15 ¹	191	31	4
W	M	17 ¹	259	60	3

¹ Selected as instructors, however, only three succeeded.

² Mentally retarded.

³ Lost 25 lb. initially but regained it when she was supposed to teach other children.

Table 11a. Results of group weight reduction program with peer group instructors

Race	Sex	Age years	Weight		
			initial, lb.	loss lb.	months
B	F	14	199.5	6.5	1
B	F	16	167	13	5
B	F	16	224	26	3
B	F	17	198	0	—
B	F	13	170	10	3
B	F	14	259	2	1
B	F	13	207	10	2
B	F	13	237	7	2
B	F	10	145	4.5	1
B	F	15	304	9	1
B	F	14	176	16	1
B	F	15	212	3	1
W	F	17	241	0	—
W	F	14	165	8	1
W	F	13	172.5	8.5	1
W	F	17	135	7	1
W	F	16	134	4	2
W	F	12	159	5	2
W	F	16	141	12	1
W	F	15	181	19	1
W	F	16	153	11	1
W	F	16	165	7	1
W	F	15	258	12	1
W	M	12	224	15	2
W	M	16	289	69	7
B	M	10	127	22	5
B	M	9	105	11	2

The four black and white boys had one male instructor, the 12 black girls had one instructor and the 11 white girls had one instructor.

changed. Two lectures were devoted to the benefits and possibilities of physical activity. Following the lectures, one group was led into the adjacent physical activity room, while the remainder of the group took a 30-min quiz on calorie counting. The groups then changed places. At the end of these 2-hour sessions, the youngsters were encouraged to continue their physical

Table IIb. Summary of table IIa

Race	Sex	Average weight, lb.	
		initial	loss
B	F	208.2	8.9
W	F	173.1	8.5
W	M	256.5	42
B	M	116	16.5
Total (all race/sex groups)		190.7	11.8

Table III. Results of individual weight reduction program during the past 7 months

Race	Sex	Age years	Weight		
			initial, lb.	loss lb.	months
W	F	15	213	33	4
B	F	16	176	22	5
W	F	17	171	12	3
W	M	13	184	22	2
W	M	13	162	32	2
W	F	15	216	9	1
W	F	15	151	20	1

activities in the training room. On the first three consecutive Sundays, all participants were invited to parties with games and non caloric refreshments in the hope to develop a group spirit. The physicians alternated in the general meetings, but as stipulated, they did not provide personalized care for any of the 27 adolescents. It is evident from table II that only 9 out of 23 (39%) black and white girls lost a significant amount of weight, i.e. > 10 lb. On the other hand, the four boys (black and white) showed a very satisfactory weight loss. Table IIb summarizes these results in the four race-sex groups.

Side-effects from the fasting days – between 1 and up to 2 days per week, depending on the degree of obesity – ranged from headaches, mild stomach upset to insomnia. These transient complaints were encountered in less than one third of the children and responded promptly to administration of aspirin, antacids or mild sedatives. We had no way of assessing the adherence

to a full fasting day among the group, whereas we had objective evidence of adherence to so-called liquid days among the adolescents in our individual treatment group through acetone testing of the urine. Usually, within 24 h of noncaloric liquid intake, the urine became 4+ positive for acetone.

In the fall of 1971, after school reopened, an additional seven adolescents started their weight reduction program. These are being managed again on an individual basis with intensive dietary instructions of mothers and children and weekly follow-up visits with review of dietary diaries. The results are presented in table III and are comparable to those obtained in the first (experimental) period.

Discussion

For understandable reasons, obese adolescents and adults are more interested in a quick weight loss rather than a prolonged weight reduction extending over years. In general, it can be stated that weight reduction in obese children and adolescents is besieged with the same difficulties as in adults since simple caloric restriction, e.g. to 1,200 or 1,000 kcal per day hardly produces any weight loss in sedentary, grossly obese individuals.

The inclusion of intermittent fasting, on the other hand, shows impressive results and is even acceptable to children when properly instructed. One to 2 days of fasting per week can be called a safe procedure if and when the protein intake on eating days exceeds the minimum requirement. With a variety of noncaloric soft drinks available (at the present time no less than 15 different brands in most grocery stores) we forced fluid intake on fasting days, advising the use of lemon and lime juice and peels to diminish the artificial taste. The first fasting day is usually followed by a marked diuresis since most obese persons are on a high sodium intake. In particular, those adolescents who managed to adhere to two consecutive 'liquid days' were rewarded with a weight loss between 4 and 6 lb. DUNCAN *et al.* [13] have attributed the occasional side-effects of transient headache, dizziness and weakness in fasting individuals to a 'sodium-depletion-syndrome', whereas dyspepsia, heartburn, 'gas pain' and mild stomach upset clearly are related to hyperacidity. It was remarkable that 70% of our young patients never felt any discomfort, and those who reported the previously mentioned transient symptoms responded to the administration of aspirin and antacids. Only one girl was unable to sleep for the first few days on the diet, but responded to a mild sedative. Insomnia has been encountered during the first

week of weight reduction among several adults over the past 2 years. A search of the literature failed to reveal any cause or explanation for this symptom.

The higher protein content of this diet also helped in minimizing the salt and fluid retention which often accompanies a high-carbohydrate diet. The sodium- and fluid-retaining capacity of dietary carbohydrates was described by BLOOM and AZAR [14] and by BORTZ *et al.* [15]. In spite of close adherence to this low-carbohydrate diet and sodium restriction, there was still a marked difference in weight loss between males and females. These differences in the two sexes are well known, and girls prior to their menstrual periods gained regularly 2–3 lb. accompanied by a general feeling of swelling and 'puffiness'. However, the extreme sensitivity to sodium intake among *obese* girls is also being observed in overweight women beyond menopause. It is not clear why obese males are much less sensitive to salt ingestion; the presence or absence of estrogen cannot explain the difference between the two sexes.

From this 16-month study, it appears that the group therapy program produced very little results, in striking contrast to the individual teaching program. Part of the explanation for this difference is to be found in our failure to recognize the detrimental effect of long (3 months) school holidays without any planned and regular group activities besides the weekly meetings. The only groups with outside activities (extended weekend trips to the ocean or mountains, etc.) were the privileged white boys and girls who had enough variety in their vacations to prevent them from boredom.

Among the adolescents in our individualized weight reduction program, it was unexpected that the academic work performance level either remained the same or improved as judged from the report cards. Each child spontaneously reported an increase in energy and no unpleasant side-effects. STANLEY *et al.* [16] similarly described improvements in school performance, group attendance, family and social relationships among successfully reducing adolescents and stated: 'The question remains whether these changes result primarily from the weight reduction itself or whether they are affected by some other factor that also helps the weight problem such as improvement of selfimage.'

In view of the health consequences of obesity in adolescence, particularly in black females, future intervention efforts must concentrate on this segment of the community. We have shown previously in the Evans County, Georgia, study [17] that overweight and continuous weight gain in adolescent black females contributed to an excess in hypertension with resulting sustained hypertensive disease and cerebrovascular complications.

From this same prospective epidemiologic study it was demonstrated that diabetes mellitus occurred in 20% of all black females but in only 7% of black males and 10% of white males and 10% of white females. Hypertension and diabetes mellitus are found with greater frequency in overweight (45 and 85%, respectively) than in normal weight individuals [18].

From our 16-month experience, we surmise the following for future intervention efforts in obese children and adolescents: (1) to individualize weight reduction; (2) to avoid starting such a program during the long summer vacations unless one can provide these children with a completely planned recreational and physical activity program simultaneously with the dietary changes; (3) to ensure availability of adequate transportation to and from the doctor's office, and (4) to check on family support and cooperation without which one may not even start a weight reduction program.

It is our belief that there are thousands of obese children in the United States who with proper instruction can be helped by an individualized program such as this.

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COMMENT ON GOAL 2

(p. 30-34)

I believe it desirable to add a brief note that patients with the so-called familial hypercholesterolemia syndrome need more detailed dietary advise (hyperlipoproteinemia type II). In addition, some qualification is indicated in the recommendation to lose weight in order to prevent ischemic heart disease, implied in the statement (p. 32): "Obesity is considered a risk factor in cardiovascular disease." But, on the same page, Dr. Cooper is quoted as stating: "Obesity aggravates cardiovascular disease." It is more of academic than practical interest to insist that obesity without diabetes, hypertension, gout, hyperlipidemia is no risk factor per se for the development of I.H.D. It is well known that smokers in general are normal weight. On the other hand, cigarette smokers have a three times higher risk to develop ischemic heart disease in comparison to non- or ex-smokers. In this connection, it is of importance to recall the results from the study of the combined effect of obesity and cigarette smoking versus normal weight and non-smoking. In the Evans County Study (see reprint) obese smokers over a seven year observation period had a risk of 150 per 1000 men for myocardial infarctions, whereas, normal weight non-smokers had a risk of 51 per 1000 men during the same observation period. There is little doubt that the well-established contribution of cigarette smoking to ischemic heart disease far outweighs the disputed contribution made by obesity.

I do not agree with the viewpoint expressed by Dr. Gori (p. 33): "As the dietary intake of fat increases, you have an almost linear increase in the incidence of breast and colon cancer," quoting as "evidence" that "other populations such as in Japan and Chile where meat consumption is low, experience also a low incidence of colon cancer." At the least, it should have been mentioned that in these two countries the major contribution to cancer mortality stems from gastric cancer. Thus, we are faced with "competing" causes of mortality. We would like to point out that there is an interesting association between fat intake and colon cancer but certainly no causal relationship. The profile of the "high risk" woman for the development of breast cancer has been described by several national and international studies and does not include obesity and fat intake. Erroneously, obesity, early onset of puberty, late onset of menopause, diabetes and hypertension were quoted (on p. 34) as principal risk factors in the development of cancer of the womb. These factors are considered of importance only in the development of endometrial cancer, i.e., cancer of the inner lining of the upper part of the uterus, but not of the cervix. Since there is some reference made to "the incidence of (colon) cancer" and its possible relation to unsaturated and saturated fats (p. 33), it appears to be indicated to present a summary of the available evidence against the hypothesis that colon cancer may be caused by polyunsaturated fatty acids (see attached review article).

LITERATURE

Heyden, Cassel, J. C.; Bartel, A.; Tyroler, H. A.; Hames, C. G. and Cornoni, J. C.: Body Weight and Cigarette Smoking as Risk Factors. *Arch. Intern Med.* 128:915, 1971.

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Body Weight and Cigarette Smoking As Risk Factors

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In males, the incidence rate of coronary heart disease (CHD) in white noncigarette smokers was 52.7/1,000 and among blacks, 9.8/1,000; among white cigarette smokers the rate was 101/1,000 but in blacks only 32.5/1,000. The incidence rate of CHD in the leanest whites was 95.5/1,000, among the leanest blacks, 24.1/1,000; however, in the most obese whites the rate was 137/1,000 and among the blacks, 53.6/1,000. When comparing white smokers with nonsmokers in the leanest and most obese tertiles, smokers run a substantial risk of developing CHD, increasing with increase in overweight (80, 90, and 150/1,000, respectively). The risk of nonsmokers developing CHD does not increase from the leanest to the moderately overweight and the most obese group, (51, 30, and 64/1,000, respectively). Therefore, obesity in white males seems to enhance the risk of CHD among cigarette smokers but not among nonsmokers.

In the seven-year follow-up study of the Evans County, Georgia, population, it was found that the rate of occurrence of new cases of coronary heart disease (CHD) was higher at each age in white males than in black males. Various analyses of these data have convinced us that these differences are unlikely to be due to vari-

ations in diagnostic criteria, to "missing" black cases, or to competing causes of death. Accordingly, attempts are being made to determine the degree to which these differences might be accounted for by differences in the distributions of some of the standard risk factors in whites and blacks. In a separate publication it has been shown that the black rates are lower than the white at comparable levels of blood pressure (both systolic and diastolic) and cholesterol levels. It is the purpose of this paper to present the findings in respect to three other factors which, with varying degrees of certainty, have been suspected to be related to CHD, cigarette smoking, body weight, and hematocrit levels.

Methods

Smoking histories were obtained on all subjects examined in the 1960 through 1962 prevalence study. In addition, all subjects had their heights and weights measured with light clothing without shoes and had a hematocrit determination using the microhematocrit centrifuge method. In all individuals judged to be free of CHD in the prevalence examination, the subsequent occurrence of new events was determined by reexamination some 87 months later and a review of all deaths that occurred between the two examinations.

Results

Cigarette Smoking.—For purposes of this analysis the population at risk was classified as either nonsmokers or smokers based upon the 1960 through 1962 smoking history. Smokers included both those who reported at

that time that they were currently smoking as well as ex-smokers. Table 1 shows that for both black and white males, smokers had higher rates of CHD than did nonsmokers but that white males had higher rates than blacks whether they were smokers or not. Thus the age-adjusted rate for white nonsmokers was 52.7/1,000, compared to 9.8 for blacks. Similarly, while white smokers had a rate of 101, the rate in black smokers was only 32.5.

Body Weight.—To take into account the joint effect of both height and weight the Quetelet index, $\frac{\text{weight}}{\text{height}^2} \times 100$ was used. Khosla and Lowe¹ determined from a study of 5,000 British males ages 15 to 64 years that this was the best index of obesity. This opinion was also confirmed by Boe et al.² The criteria for their choice was that the index be highly correlated with weight but independent of height. To provide convenient categories for analysis, the distribution of the Quetelet index for all males was divided into equal tertiles. This distribution ranged from a value of 2.121, which was the value for the leanest man, to 6.163, for the most obese man. The first tertile included all men with a Quetelet index of less than 3.244. The second tertile included all men whose index ranged between 3.244 and 3.697 and the third tertile was those men with an index of 3.698 or greater.

As shown in Table 2, there was a modest relationship between body

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size and incidence of CHD in both blacks and whites. While no gradient occurs, whites in the third tertile of the Quetelet index range have an age-adjusted rate 1.43 times as great as those in the first tertile. In blacks the relative risk of being in the third as opposed to the first tertile is 2.22. In each tertile, however, at each age, whites have higher rates than do blacks.

Hematocrit Level.—Considerable controversy exists as to whether blood viscosity, as measured by hematocrit levels, constitutes a risk factor in CHD. Ample physiological evidence exists which would make such a relationship seem plausible. Polycythemia is known to predispose to thrombus formation²; reduction in myocardial blood flow occurs when anemic patients are transfused to polycythemic levels⁴ and such variations in coronary flow which follow alterations in blood viscosity may be of clinical significance in a setting of atherosclerotic disease.⁵

Studies attempting to document the added risk that high blood viscosity (at least as measured by hematocrit levels) might have for the development of CHD, however, have yielded conflicting results.

Burch and DePasquale found that the hematocrit levels in both male and female patients with myocardial infarction was higher than in controls matched for age-ethnic group and social-class level.⁶ These results were confirmed by Mayer in a study of 66 men with coronary disease and 68 controls of the same age and sex.⁷ Conley and co-workers did not find any differences between 200 male private patients with acute myocardial infarction and 915 "normal" individuals (including 721 medical students, 136 business executives, and 58 airline pilots).⁸ McDonough et al similarly found no difference between cases and controls as far as hematocrit values are concerned.⁹

In part these conflicting results

Table 1.—Incidence of CHD by Cigarette Smoking History, Age, and Ethnic Group*

Age (yr)	White Males			Black Males		
	No.	Cases	Rate/1,000	No.	Cases	Rate/1,000
Nonsmokers						
15-24	62	0	...	16	0	...
25-34	28	0	...	12	0	...
35-44	35	0	...	21	1	48
45-54	68	4	59	40	0	...
55-64	67	4	60	31	0	...
65-74	46	9	196	34	1	29
75+	1	0	...	3	0	...
All ages	308	17	55	157	2	13
Age-adjusted rate			52.7			9.8
Smokers and Ex-Smokers						
15-24	40	0	...	30	0	...
25-34	67	0	...	24	0	...
35-44	125	10	80	55	0	...
45-54	181	15	83	126	7	56
55-64	88	16	182	56	1	18
65-74	44	12	273	30	3	100
75+	5	2	(400)	1	0	...
All ages	550	55	100	322	11	34
Age-adjusted rate			101			32.5
Unknown Smoking Status						
15-24	16	0	...	35	0	...
25-34	14	0	...	7	0	...
35-44	5	0	...	3	0	...
45-54	0	0	...	0	0	...
55-64	0	0	...	0	0	...
65-74	0	0	...	0	0	...
75+	0	0	...	1	0	...
All ages	35	0	...	46	0	...

* Eighty-seven-month follow-up period (males only).

may be accounted for by the difficulties of interpretation that so often accompany any case-control study. These include the effect of the myocardial infarct itself on the hematocrit levels, the adequacy of the controls used, and the problem of selective survival. ("Cases" in such a study are restricted to those who have survived their infarct. Conceivably, individuals with the highest hematocrit values who develop a myocardial infarct may be the ones who die, leaving only those patients with relatively low hematocrit levels available for study.) These problems are to a large extent overcome by prospective or cohort studies, and it is of interest that in the Framingham study, where these phenomena were studied prospectively, both elevated hemoglobin and hematocrit levels were shown to

increase the risk of subsequent CHD.¹⁰

The findings from this study (Table 3) confirm the Framingham findings as far as white males are concerned. The relative risk of a hematocrit level of 50% or greater compared to one of 40% or less was 2.3 (113 cases/1,000 compared to 49 cases/1,000). No such relationship could be observed for blacks, however; also, as in the previous analyses the white rates were higher than the black rates at each level of hematocrit.

It is thus apparent that, as in the case of blood pressure and cholesterol level, black males in Evans County have a lower incidence rate of CHD than do white males at each level of risk factors (cigarette smoking, Quetelet index, and hematocrit value). While the rates in blacks seem

to respond to variations in all of these risk factors in a manner similar to whites (with the exception perhaps of hematocrit level), it would appear that some additional factors must be operative which are protective for blacks. As is shown in a subsequent paper, at least one of these additional factors may be sustained and ex-

cessive physical activity.

Up to this point the relationship of these risk factors to CHD incidence has been examined one at a time. In view of the potential importance of some of the factors (particularly smoking, body weight, and blood pressure) for intervention purposes, it was decided to determine the com-

bined effects of some of these. While this could not be accomplished for blacks (due to the small number of cases) and, thus, could not contribute any further explanation to the black-white difference, analyzing the relationship in white males only could produce some useful information.

Cigarette Smoking and Body Weight.—In this and subsequent analyses the classification of men into Quetelet index tertiles was recomputed using the distribution of Quetelet index in white males only. As no comparisons were to be made with black males, it was considered that this would provide a more appropriate basis for comparison than the intervals based on the distribution of Quetelet index in all males (black and white) used in the previous analysis. While this reclassification results in a slightly different absolute value for the incidence rates, the relationship between Quetelet index and CHD shown in Table 2 remains unchanged.

One of the reasons for examining the combined effects of body weight and cigarette smoking on incidence was the suspicion we had that the relationship of body weight to CHD could be masked if many of the heavier men had gained weight as a consequence of having given up smoking. Under such circumstances any deleterious effect that overweight might have could conceivably be counterbalanced by cessation of cigarette smoking. Alternatively, the possibility exists that any beneficial effect of giving up smoking might be nullified if there was a subsequent weight gain.

It should be borne in mind that this analysis can at best only provide suggestive answers to these questions as we do not as yet have data showing the incidence of CHD in those individuals whose weight or cigarette smoking patterns have in fact changed. What is available is the subsequent incidence of CHD in those individuals who in 1960 were both over-

Table 2.—Incidence of CHD by Quetelet Index, Age, and Ethnic Group*

Quetelet Index	Age (yr)	White Males			Black Males		
		No.	Cases	Rate/1,000	No.	Cases	Rate/1,000
First tertile	35-44	50	1	20	24	0	...
	45-54	58	4	69	41	1	24
	55-64	53	5	94	29	0	...
	65-74	32	8	250	22	2	91
	75+	1	1	(1,000)	1	0	...
	All ages	194	19	98	117	3	26
	Age-adjusted rate			95.5			24.1
Second tertile	35-44	53	2	38	30	1	33
	45-54	76	5	66	74	2	29
	55-64	48	7	146	34	0	...
	65-74	28	4	143	20	0	...
	75+	4	1	(250)	3	0	...
	All ages	209	19	91	157	3	19
	Age-adjusted rate			91.3			19.2
Third tertile	35-44	63	7	111	25	0	...
	45-54	115	10	87	55	4	73
	55-64	54	8	148	24	1	42
	65-74	30	9	300	22	2	91
	75+	1	0	...	1	0	...
	All ages	263	34	129	127	7	55
	Age-adjusted rate			137.0			53.6

* Eighty-seven-month follow-up period (males, 35 years of age and older).

Table 3.—Incidence of CHD by Hematocrit Level and Ethnic Group*

	Hematocrit Value					
	40%		41% to 49%		50%	
	No.	Cases	No.	Cases	No.	Cases
White	27	2	700	51	137	14
Black	58	2	411	11	40	0

* Eighty-seven-month follow-up period (males only).

Table 4.—Age-Adjusted Incidence Rates of CHD by Quetelet Index and Cigarette Smoking*

Smoking Status at Entry Into Study	Quetelet Index at Entry Into Study								
	First Tertile			Second Tertile			Third Tertile		
	No.	Cases	Rate	No.	Cases	Rate	No.	Cases	Rate
Smokers†	183	15	80	161	14	90	127	16	150
Nonsmokers	90	5	51	99	3	30	119	9	64

* Eighty-seven-month follow-up period (white males only).

† Smokers include only those who were smoking cigarettes in 1960. Ex-smokers have been excluded from this table.

weight for their age and height and who smoked cigarettes compared to those with similar weight who did not smoke cigarettes.

Bearing this in mind Table 4 does suggest that part of the effect of increased body weight is indeed being disguised by cessation of cigarette smoking. Lean men (first tertile) who smoke have an age-adjusted incidence rate of CHD of 80. Heavy men who do not smoke (third tertile, nonsmokers) only have a rate of 64. By contrast equally heavy men who are smokers have a rate of 150. These latter men obviously have gained weight without giving up smoking. If they had given up smoking their risk of developing CHD presumably would approximate the third tertile nonsmokers (ie, 64) and would, thus, be very different from lean (first tertile) men.

The degree to which the beneficial effect of giving up smoking is mitigated by subsequent weight gain is less clearly demonstrated in Table 4. As mentioned above lean men who smoke (first tertile, smokers) have an incidence rate of 80. If they stop smoking but gain weight, the assumption is that their rate might drop to that of the nonsmoking third tertile men (64). If they stop smoking but do not gain weight they might have a slightly greater reduction in risk to 51 (nonsmokers, first tertile).

The Relationship of Body Weight and Blood Pressure to Coronary Heart Disease

The question of the joint relationship of elevated blood pressure and overweight to CHD is a subject of some controversy. While it is well recognized that a high correlation exists between body weight and blood pressure, no unanimity of opinion exists concerning the possible effect that variations in body weight might have on the prognostic significance of elevated blood pressure.

For over a decade actuarial data

Table 5.—Age-Adjusted Incidence Rates of CHD by Quetelet Index and Systolic Blood Pressure*

Systolic BP at Entry Into Study	Quetelet Index at Entry Into Study							
	First Tertile			Second Tertile			Third Tertile	
	No.	Cases	Age-Adjusted Rate/1,000	No.	Cases	Age-Adjusted Rate/1,000	No.	Cases
≤139	193	6	44	179	9	63	140	7
140-154	64	5	78	61	4	70	78	11
≥160	45	11	123	54	7	75	74	12

* Eighty-seven-month follow-up period (white males only).

have demonstrated the excessive mortality risk in overweight persons with high blood pressures. However, several studies of hypertensive patients in clinical series have shown conflicting results. Bechgaard,¹¹ Frant and Groen,¹² and Mathisen et al¹³ found mortality in obese hypertensive subjects no higher than in nonobese hypertensive persons. Breslin et al¹⁴ in a study of 14 patients with one or more retinal exudates, with or without hemorrhage, but with no papilledema, found that the survival rate was actually better in obese than in nonobese patients. In hypertensive patients without these retinal changes there was no difference in survival between obese and nonobese. The authors concluded at the very least that obesity did not seem to have an adverse effect on the survival in hypertensive patients.

A Japanese study examined the prognostic significance of hypertension in the obese and nonobese by dividing hypertensive patients into five groups according to the percent deviation of their body weight on admission from standard body weight for height. Four-year mortality rates of each group were compared. Average ages and overall severity of hypertension of these five groups were similar. The four-year mortality rates of these five groups were 4.5% in the most obese group (20% or more overweight), 12.5% in the slightly obese group (11% to 19% overweight), 13.0% in the standard weight group, 4.2% in the slightly emaciated group (11% to

19% underweight), and 25% in the most emaciated group (20% or more underweight). The authors could provide no explanation for the better prognosis in the most obese group and the worst prognosis in the most emaciated group.¹⁵

On the other hand, in two prospective studies^{16,17} and in a retrospective study by Levy et al,¹⁸ it was clearly shown that overweight and hypertension are associated with an excess of coronary disease and cerebrovascular disease, especially among men. Severity of hypertensive retinopathy and cardiovascular complications were related to obesity of Tibblins' study of hypertensive disease in men aged 50 years.¹⁹

This phenomenon was examined in the current study by examining the seven-year incidence of CHD in men classified by their Quetelet index and level of systolic blood pressure in 1960 through 1962.

As can be seen for Table 5, the data tend to support the conclusions of the Japanese study.¹⁵ The relative risk of hypertensives developing CHD in lean men (first tertile) is 2.8 times that of normotensives (incidence of 123 and 44, respectively). In the most overweight third, by contrast, the relative risk of hypertension is only 1.5 (incidence of 107 compared to 71). One possible explanation for these findings may be in the degree of hypertension suffered by the lean as compared to the overweight. In Table 5 the population is stratified into only three blood pressure groups. It is

quite possible that the lean men with systolic blood pressures of over 160 mm Hg have considerably higher levels than the overweight men in this category.

Table 5 also produces some suggestive evidence in another aspect of this problem, the effect of weight reduction combined with the reduction of blood pressure compared to the consequences of reduction of blood pressure levels alone. According to these data reduction of systolic blood pressure from over 160 mm Hg to under 140 mm Hg without any change in weight might be expected to reduce the risk of CHD in overweight men from 107 to 71 (these being the relevant incidence rates in men in the third Quetelet index tertile). Reduction of blood pressure levels and weight reduction, however, might be expected to lower the risk of CHD from 107 to that of first tertile men with blood pressure under 140 mm Hg, ie, an incidence rate of 44. This of course is but confirmation of a well established clinical impression which makes all the more surprising the lack of attention that weight reduction has received in intervention studies concerned with reducing blood

pressures in the hope of preventing cardiovascular complications.

Comment and Conclusions

In this seven-year follow-up study in Evans County, further evidence is produced which shows that black males in this county are at lower risk of developing CHD than are white males, regardless of the level of risk factors. Thus, at comparable levels of body weight and hematocrit level and whether smokers or nonsmokers, black males had age-adjusted incidence rates of CHD which were only one third to one fifth those of white men. In spite of the small number of cases available for analysis in the blacks, their rates did seem to respond to variations in these risk factors in a manner similar to whites (with the possible exception of hematocrit value) but always at a lower level. It would thus appear that, while these risk factors do affect blacks in a manner similar to whites, some additional factors must be operative which either enhance the effect of the risk factors in whites or protect blacks from some of their consequences. As is shown in a subsequent paper, at least one of these

additional factors may be sustained and excessive physical activity.

In addition to exploring black-white differences, the joint effects of cigarette smoking and body weight and systolic blood pressure and body weight on the subsequent development of CHD in white males was examined. The data would tend to support the following:

1. The deleterious effect of overweight could be masked if many overweight men in a study had achieved this status as a result of discontinuing smoking.

2. Despite the high correlation known to exist between body weight and hypertension, when systolic hypertension occurs in lean men, it is of graver prognostic significance (as far as subsequent CHD is concerned) than hypertension in overweight men.

3. While reduction of blood pressure levels alone in overweight men can be expected to have a modestly beneficial effect on preventing the occurrence of CHD, the reduction of weight together with lowering of blood pressure in such individuals can be expected to have considerably greater effect.

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Editorial

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Polyunsaturated Fatty Acids and Colon Cancer

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The question of undesirable side effects from the long-term use of a low cholesterol diet with emphasis on polyunsaturated fats briefly developed into a major public concern after the publication of an article 'Incidence of Cancer in Man on a Diet High in Polyunsaturated Fat' (5). In their 8-year double-blind trial of a diet high in polyunsaturated vegetable oils and low in saturated fat and cholesterol, 174 deaths were noted in the experimental group and 178 deaths in the control group. Thirty-one of the 174 deaths in the experimental group were due to cancer as opposed to 17 of 178 deaths in the control group. The authors concluded that it is 'premature to make a blanket prescription of a diet high in polyunsaturated fat for the entire population', implying that their data could mean that the polyunsaturated fatty acid diet might have had a co-carcinogenic effect in the experimental group. However, a review of the table showing adherence to diet in patients with fatal carcinomas during the diet phase clarifies the situation and removes any doubt that the diet high in polyunsaturated fats might have had anything to do with carcinogenesis or co-carcinogenesis (table I). Not less than 12 cases of fatal carcinoma were found in persons who adhered less than 20 % of the time to the experimental diet (adherence, calculated from attendance records, was expressed as a percentage of the maximum number of meals which could have been taken in the study dining-hall). Only 19 persons from the experimental group died with cancer and adhered to the prescribed diet between 20 and 100 % during the 8-year observation period. This leaves 17 cancer cases in the control but only 19 cases in the experimental group, which practically means that the claimed statistically significant difference is removed between these two groups of people. The 12 men who were listed in the experimental group but did adhere only very occasionally to the prescribed diet (less than 20 % within the 8-year observation period) can hardly be called dieters. It was not surprising, therefore, that another group of four investigators (1) found that the results of their studies 'are consistent with the hypothesis that the cholesterol-lowering diets do not influence cancer risk'.

Table 1. Adherence to diet in patients with fatal carcinoma during the diet phase

Adherence, %	Control group	Experimental group
0-10	2	10
10-20	1	2
30-40	0	0
40-50	3	3
50-60	3	3
60-70	0	4
70-80	2	2
80-90	4	1
90-100	1	3
<i>Total</i>	<i>17</i>	<i>31</i>

From *Pearce and Dayton* (5).

For the purpose of this discussion, another aspect of the article by *Pearce and Dayton* (5) appears of great importance. *Regardless of adherence or non-adherence to the diet, these authors reported five cases of 'digestive and peritoneal cancer' in the control group and six cases of 'digestive and peritoneal cancer' in the experimental group during the diet phase. During the 2-year period after termination of the diet (the so-called post-diet phase), four cases of 'digestive and peritoneal cancer' were observed in the control group and three cases in the experimental group. 'Digestive and peritoneal cancer' excluded all stomach cancers specifically, which leads us to conclude that there were no differences in the occurrence of colon-rectum cancer between controls and experimental persons either in the dietary phase or the post-diet phase. Even Pearce and Dayton (5) admitted that 'many of the cancer deaths in the experimental group were among those who did not adhere closely to the diet. This reduces the possibility that the feeding of polyunsaturated oils was responsible for the excess carcinoma mortality observed in the experimental group.'*

Colon cancer and blood-cholesterol. The ultimate question to be asked of serum-cholesterol-lowering diets is, are lives being saved or endangered? At this stage of our knowledge, we would agree with the editorial view of the *Brit. Med. J.* (2): 'No convincing case has been made that polyunsaturated fatty acid diets cause either premature ageing or cancer.' However, a new dimension was added when *Rose et al.* (6) ventured into a most fascinating aspect of cancer epidemiology: in a retrospective study of 90 cases of colon cancer, pooled from several long-term studies, he wanted to find out whether serum-cholesterol-concentrations would predict colon cancer. The finding:

'The initial levels of blood-cholesterol in these men were found surprisingly to be lower than the expected values.' Although the authors were quick to point out that 'the data do not provide an ideal test of an association between blood-cholesterol and colon cancer', they chose to interpret their data that the colon cancer patients were individuals with lower levels of blood-cholesterol who tended to form more bile salts 'perhaps in part as a result of their higher intake of polyunsaturated fatty acids. This would increase the amount of substrates available for the carcinogen-forming bacteria, and hence increase also the risk of colon cancer. The negative association between blood-cholesterol level and colon cancer risk might rise if in some individuals the intestine were more extensively colonized with bile-degrading bacteria, perhaps as a result of a higher intake of polyunsaturated fat or a lower intake of fibre. ... There is need for further study of the relation in individuals between carcinogen-producing faecal bacteria and the dietary intake of polyunsaturated fat and fibre.'

This, in my opinion, is a rather strong statement not warranted by the actual data. Firstly, colon cancer belongs to a group of malignant diseases with a rather slow progression and relatively favorable 5-year survival rates. The 1974 Cancer Facts and Figures of the American Cancer Society unfortunately lump rectum and colon cancer together. Five year cancer survival rates are quoted as 69 % in localized cases and 39 % in cases with regional involvement. The chances to survive early diagnosis of colon cancer, surgery and/or radiation therapy are certainly better than in bronchogenic, gastric, ovarian or renal cancer, to name only a few.

For the reasons mentioned it appears to be of paramount importance to investigate the alleged association of low cholesterol levels and cancer development among the 90 men. I therefore posed the question to Dr. *Rose* how many of them had their cholesterol determination within 5 years prior to death from colon cancer. As it turned out, there were 48 patients — that is more than 50 % of the total number of colon cancer patients — who died within 5 years after the cholesterol determination. If we accept the experience by oncologists that colon cancer, in comparison to other more aggressive malignancies is a relatively slow progressing type of cancer, we can assume that people dying within 5 years of their last cholesterol determination must have had either regional involvement or wide-spread metastatic disease. Dr. *Rose* kindly provided me with a table (table II) demonstrating the interval from screening to death from colon cancer. I would like to submit that at least in those cases dying within the 5-year period, the cholesterol level would have to be below expectation. Particularly in colon cancer, a history of ulcerative colitis may have existed in at least a few of these patients with colon cancer and may have contributed to the 'lower-than-expected' cholesterol levels. Severe anorexia may appear long before any obvious contributing cause such as intestinal obstruction and again would have explained lower-than-expected cholesterol levels. The three most common systemic effects (4) of malignancies are: anorexia, increased basal metabolic rate, negative nitrogen balance. In contrast, only 'few instances of lowered basal metabolic rate with active malignancy have been reported. In some patients the rate is within

Table II. Cholesterol levels and colon cancer

Interval from screening to death (years)	Number of cases	With cholesterol level below expectation, %
< 2	13	77
2-3	20	60
4-5	15	53
6-7	11	82
8-9	5	40
> 10	26	62
	90	63

From *Rose*, personal communication, 1974.

normal range but usually it is greatly increased'. A classical description (8) of the cachectic cancer patients may have well fitted those 33 cases of colon cancer who died within 1-3 years after their cholesterol determination: 'Marked asthenia, significant loss of body fat (!), protein and other components, anemia, water and electrolyte abnormalities and increased basal metabolic rate and energy expenditure despite the reduced dietary intake - just the most obvious manifestations of a profound systemic derangement of the host metabolism.' These well-known facts would conveniently explain the lower than expected cholesterol values for at least one-third of *Rose's* patients.

A review of the literature (9) revealed no difference in dietary fat intake between colon cancer patients and controls. This particular study added little to the prevailing controversy since all cancer patients were studied after diagnosis of colon cancer: nine male patients had cholesterol levels below 200 mg%, nine patients had cholesterol levels above 200 mg%.

Dr. *Rose* added in a personal communication 'that the cholesterol deviation to lower levels is greater when the interval from screening to diagnosis is short, i.e., in sick men. If we take out the men found within 1 year to have cancer, there is not in the remainder any correlation between cholesterol deviation and interval to diagnosis.' Even if an association between low cholesterol levels and the development of cancer of the colon would present a causal relation (which by no means can be deduced from the data presented), it would be an unfortunate mistake to create the impression that polyunsaturated fats might even be implicated in the development of colon cancer. Aside from the problem of retrospective dietary intake studies, there was not even an attempt made to document an increase in the use of polyunsaturated fat within the various epidemiological studies over the past decade. *Higginson* (3) found no differences in

the regular use of vegetable or animal fat in a retrospective study among 340 patients with carcinoma of the colon and rectum and 1,020 controls: 55.6 % cancer patients and 56.6 % controls used butter; 77.4 % cancer patients and 75.4 % controls used margarine; 19.7 % cancer patients and 18.6 % controls used lard; 81.8 % cancer patients and 80.5 % used vegetable shortening; 50.9 % of both groups used vegetable oils.

Neither the study by *Pearce and Dayton* (5), quoted previously, nor the long-term results from the 'Anti-Coronary Club' (7) give any suggestive hint in support of the hypothesis advanced by *Rose et al.* (6): the 13-year experience of the Diet and Heart Disease Study conducted by the New York City Health Department concluded: 'Our observations lend no confirmation to the alleged association between excess cancer mortality and high polyunsaturated fatty acid diet.' In brief, 1,764 men, 40–59 years of age, have come under long-term observation: (a) a control group of 533 men; (b) an active experimental group of 378 men keeping a relatively high polyunsaturated fatty acid diet, and (c) an inactive experimental group of 853 men who were once active subjects but now limit their participation to appearance at the study facilities annually for physical examination to ascertain the status of study end-points. The results of the 13-year observation period are presented in table III.

Six cases of 378 *active dieters* amount to a *cancer incidence of 1.59 %*; 15 men with cancer of 853 *inactive persons* amount to a *cancer incidence of 1.75 %*; ten cases of cancer of 533 *controls* equal a *cancer incidence of 1.88 %*. The slightly lower risk of the active dieters to develop cancer agrees well with

Table III. Number of deaths by study group by cause as of September 1970 (A.C.C.)

Cause	Experimental		Control
	active	inactive	
Heart disease ¹	30	58	10
Cancer	6	15	10
Other	5	12	5
<i>Total</i>	<i>42</i>	<i>85</i>	<i>25</i>
Person-years of observation	5,903	6,156	4,372

From *Singman et al.* (7).

¹ Includes the group of subjects who entered the study with prior overt coronary heart disease. These subjects have never been included in prior reports since they could not add to the experience concerning new coronary heart disease. However, they have been included here since they can contribute to cancer experience.

Table IV. Number of deaths from cancer by study group by site, June 1957 to September 1970 (A.C.C.)

Site	Experimental		Control
	active ¹	inactive	
Esophagus	1		
Stomach			3
Colon	1	3	1
Rectum		1	
Pancreas	1	1	
Liver		1	1
Larynx		1	
Lung	1	3	1
Prostate		1	
Spine	1		
Brain	1	1	1
Lymphosarcoma		2	2
Leukemia			1
General peritoneal		1	
Total	6	15	10

From Singman *et al.* (7).

1 Cases of cancer in inactive subjects developing within 6 months of becoming inactive have been charged to the active group.

Table V. Expected and actual number of deaths from cancer by entry age by study group (A.C.C.)

Group	40-49		50-59	
	observed	expected	observed	expected
Experimental				
Active	0	1.6	6	23.3
Inactive	0	3.1	15	19.7
Total	0	4.7	21	43.0
Control	2	3.6	8	13.2

From Singman *et al.* (7).

the previously quoted article by *Ederer et al.* (1) in the combined experience of the studies from Oslo, London, Helsinki and Faribault, the occurrence of cancer (total of diet and post-diet phase) was 7.7 % in the experimental group and 10.9 % in the controls. Again, the 'Anti-Coronary Club' does not support the hypothesis proposed by *Rose et al.* (6) (table IV): from a total of 31 deaths from cancer observed between June 1957 through September 1970 only one cancer of the colon occurred in the experimental actively dieting group, three occurred in the inactive group and 1 in the control group. Table V reveals the expected and actual number of deaths from cancer. In the age group 40-49 years not a single case of cancer was observed in the active or inactive experimental group. However, in the age group 50-59 years, the observed cancer deaths in the active experimental group was four times lower than expected. In the inactive experimental group and in the control group the observed cancer deaths were much closer to the expected number of deaths.

Conclusion

The evidence presented thus exculpates polyunsaturated fatty acid diets from causing cancer. In answering the specific question raised by *Rose et al.* (6) about the possible association of high polyunsaturated fat diets and the development of colon cancer, the quoted results from the 'Anti-Coronary Club' and the study by *Pearce and Dayton* (5) (regarding 'digestive-peritoneal cancers' among 'dieters' and controls) speak for themselves. We would agree with *Keys* who wrote in a personal communication: 'It still seems mysterious what the cholesterol-colon cancer data reflect and mean. Associations that emerge from purely statistical analysis, with no basis of pathogenetic theory or support from experiment, may be the clue to other researches of importance, but by themselves may have no meaning.' While there is an abundance from the recent literature to support the hypothesis that the decreased intake of fibre (slowly absorbed carbohydrates) and consequently decreased bowel-transit time is markedly associated with the high incidence of colonic cancer in the Western countries, the impression that polyunsaturated fatty acid diets might be implicated in colon cancer has no support either from clinical experience, epidemiological research or experimental studies.

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COMMENT ON GOAL 3 AND 4

(p. 35-42)

The eight pages on "reduction of saturated fat consumption" and "cholesterol consumption" summarize very well the state of the art. Whereas the British counterpart of the U.S. Senate Report (Report of the Advisory Panel of the Committee on Medical Aspects of Food Policy on Diet in Relation to Cardiovascular and Cerebrovascular Disease, Department of Health and Social Security, London, 1974) was concerned with the soft water theory¹ on cardiovascular disease development and dismissed the recommendation for an increased use of polyunsaturated fatty acids in the diet, the U.S. Senate Report came forward with an unequivocal statement on the desirable distribution of saturated, monounsaturated and polyunsaturated fatty acids in the future American diet. We would add only one more sentence: Since it is unlikely that most Americans will reduce their total fat consumption to 30 percent of the caloric intake, it should be considered to substitute more saturated fatty acids by polyunsaturated fats. The goal, then, would be to decrease saturated fats to less than 10 percent and the polyunsaturated fats to more than 10 percent of the total caloric intake. This would mean: (a) higher fish consumption, (b) enrichment of skim milk products with polyunsaturated oils, (c) development of margarines with a 50 percent polyunsaturated fatty acid content (whereas, most margarines do not contain more than 35 percent as PUFA).

There is considerable experimental evidence on the functions of linoleic acid, with particular reference to its antithrombotic tendencies and to prostaglandin production. Because of these properties, as well as its effectiveness in lowering cholesterol levels, many scientists recommend replacement of dietary SAFA as much as possible by linoleic acid, as a positive move rather than merely as a substitution. I would go along with this viewpoint expressed recently by A. G. Shaper and J. W. Marr: Dietary recommendations for the community towards the postponement of coronary heart disease. *Brit. Med. J.*, 1:867, 1977.

It is appreciated that very little has been said about triglycerides, and its alleged role in coronary atherogenesis. Our literature review is enclosed.

The presently available dietary experiments have been summarized in the enclosed chapter: "Epidemiological Data on Dietary Fat Intake and Atherosclerosis" (p. 69-77). In addition, we have shown the dietary changes taking place in the community of Evans County, Georgia and their influence on cholesterol levels (p. 77-83). An overview of epidemiological evidence linking hypercholesterolemia and the incidence of ischemic heart disease as well as chapters pertaining to gout, diabetes, hypertension and obesity in relation to coronary disease are presented in the book: "Risk Factors of Ischemic Heart Disease."

¹ Enclosed is our recent literature review of this topic.

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THE HARD FACTS BEHIND THE HARD-WATER THEORY AND ISCHEMIC HEART DISEASE

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INTRODUCTION

THE FOLLOWING viewpoint in the official **Journal of the American Medical Association** reflects a summary of reports over the past 18 yr after Kobayashi in 1957 [1] had observed a negative correlation between hardness of drinking water and death rates from apoplexy, and Schroeder in 1960 [2] had extended this finding to a likewise negative correlation for hypertensive and arteriosclerotic heart disease:

"As evidence accumulates, it looks more and more likely that there is something, either in the drinking water or closely associated with the drinking water, that affects the rate of heart attacks and stroke in this country and in many others...it might be reasonable to urge caution on those with hard-water supply who wish to soften their water. In particular, those in hard-water areas who do soften their water supplies might regard it judicious to leave one tap still producing hard water for drinking". [3]

However, two other articles, published within the same 4-week period late in 1974 on this topic took exception to the hypothesis [4, 5]. They support our suspicion that official British recommendations [6] to seriously consider the 'water story' as contributing to the development of ischemic heart disease are premature and, at best, ill-founded. The study by Nixon and Carpenter [4] concluded that, "when socio-environmental factors and water hardness were allowed for, no significant associations emerged". Similarly, a study conducted in three Los Angeles communities [5] was summarized: "The study does not support the hypothesis that mortality from cardiovascular disease and infant and neonatal mortality are related inversely to hardness of drinking water". Our own interest in this question was kindled through the epidemiological study of Tyroler [7] in North Carolina, which is part of the cardiovascular and cerebrovascular disease belt of the United States, commonly referred to as the 'stroke belt' of the United States. The highest cardiovascular death rates were found in the Eastern seaboard coastal plains with water of intermediate hardness, while the Western North Carolina mountainous

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region had the *softest* water and the *lowest* death rates. Thus, earlier reports from England and the United States could not be confirmed in one geographical region where the theory could have proven crucial for preventive action, e.g. hardening of the water supply.

This review is intended to bring the reader up to date with the prevailing controversies and to demonstrate the difficulty of the promoters of the hypothesis to provide any biological explanation for the mechanism of the alleged protective influence of hard water on cardiovascular disease or death from it.

CLAIMS BY THE PROPONENTS OF THE WATER HYPOTHESIS

In the 1974 Report of the Advisory Panel of the Committee on Medical Aspects of Food Policy (Nutrition) on Diet in Relation to Cardiovascular and Cerebrovascular Disease [6], a British panel of 19 experts in the field allotted Professor Yudkin a lonely place for a minority report in a so-called Note of Reservation in which he was able to voice his unfounded concern regarding the role of sucrose in the etiology of ischemic heart disease. But the Report also produced a surprise by shifting present worldwide research emphasis from fat to water: The 'dietary characteristics which were considered as possible risk factors for ischemic heart disease' included overconsumption of food, excess of dietary fat, polyunsaturated versus saturated fatty acids, excess of dietary cholesterol, high consumption of common salt, deficiency of dietary fibre and softness of the water supply. While it was explicitly stated, that "*there is no certainty that reduction of cholesterol in the serum diminishes the susceptibility to I.H.D.*" and whereas 'the Panel was unanimous in remaining unconvinced that the incidence of I.H.D. in the United Kingdom would be reduced in consequence of a rise in the ratio of polyunsaturated to saturated fatty acids in the diet', the so-called 'water story' was given serious consideration. The Panel recommended "*that any proposals for softening the water supply in any part of the country should be considered in the light of knowledge about the observed positive relationship between the death rate from I.H.D. and the softness of the local water supply*". One full page in this 23 pp. report was devoted to water:

"During the past 15 years investigators in several countries have observed a negative association between the hardness of the domestic water supply and the local death rate from cardiovascular disease (cerebrovascular, coronary or other heart disease)—that is to say, the harder the water supply the lower the death rate from cardiovascular disease. This association also holds for areas within the U.K. With respect to known substances in the water supply, the strongest negative association of the death rate from cardiovascular disease is with the content of calcium and temporary hardness (the bicarbonate fraction of total hardness)... In areas where, in the past, the water supply had been softened the introduction of softening was usually found to be followed by greater increase in the death rate from cardiovascular disease than occurred in areas where the water supply had been left unchanged. Conversely, where the water supply had become harder any rise in the death rate was in general less than that seen in areas where the hardness of the water supply remained unaltered".

The recent literature is indeed replete with statements such as: "It is now established that there is a statistical association between mortality, in particular from cardiovascular disease, and the hardness of drinking water" [8], or: "It is well known that there is a negative correlation between atherosclerotic heart disease and hardness of the finished drinking water" [9], or: "Regional death rates from

I.H.D. in several countries have found to be inversely related to the hardness of the local water supply. British studies have demonstrated that this relation is not secondary to other variables such as climate and socio-economic factors, and that calcium is the water component most closely correlated with the variation in death rate" [10]. Undoubtedly, research in factors associated with the underlying causes of ischemic heart disease has to continue in many different directions and any new hypothesis must be welcomed. But it is quite another development if we are going to disregard the importance of past and ongoing research in established and most promising dietary factors and leave undisputed wide-reaching official recommendations from a group of British experts which may influence food manufacturers, government officials as well as physicians and consumers in the Western world. An examination of the existing body of evidence in favor of the 'water story' reveals inconsistencies and controversies that it appears premature to agree with the conclusions which have been embodied in the COMA-Report [6].

CRITIQUE OF THE PREVAILING THEORIES

To begin with, the 'experiment of nature' which held the greatest promise of demonstrating a measurable impact on cardiovascular mortality and which was quoted in the COMA-Report, cannot be accepted at face value. Changes in the death rates between 1950-61 of the large towns of England and Wales where the hardness of the water supply has undergone differences in degree of hardness for a variety of reasons during the past 30 years were studied by Crawford *et al.*, 1971 [8]. An increase or decrease of 'around' 50 ppm was accepted as sufficient indication of a change in hardness, but in no town had hardness changed from very hard to soft, or vice versa. Roberts and Lloyd, 1972 [11] take exception to the study design and the conclusions reached from the statistical analysis: "Eleven out of 83 towns satisfied the quoted criteria of change (in 5 hardness increased, in 6 hardness decreased). Crawford *et al.* claimed that, in general, in towns where the water had become harder, the effect on cardiovascular death rates had been favorable (i.e. deaths in males had risen at less than the average rate, and deaths in females had decreased at greater than the average rate); however, out of 8 changes in cardiovascular mortality observed, only two were statistically significant at nominal levels only...Crawford *et al.* admitted that these data on water hardness were crude, and this makes us wonder if a change of 50 ppm is large enough to test the proposed hypothesis adequately. Secondly, Crawford *et al.* did not consider the initial value of the independent variable, so that even after a change, 'softened' towns tended to have harder water than did 'hardened' towns. Thirdly, towns where the water became softer, were different in other ways (e.g. social class composition) from towns where it became harder." This represents a most valuable argument since all over the Western world (e.g. Evans County Study 1971 [12], Pell and D'Alonzo, 1970 [13], Hinkle *et al.*, 1969 [14]) including the U.K., the I.H.D. mortality rates have changed remarkably from a preponderance in the upper social class in the early fifties to a reversed trend in the early sixties due to a proportionately greater increase in mortality in the lower social class. In Crawford's study the 'softened' towns were much more industrialized than the 'hardened' towns. Roberts and Lloyd's proposition that the observed changes in

cardiovascular mortality arose, not out of earlier changes in water hardness but of difference in social-class composition therefore carries more credibility.

Even if it were assumed that there was some association between water hardness and cardiovascular disease, the 'calcium content' of water—pointed out as the factor under consideration in the COMA-Report—could not possibly hold up as decisive for four reasons:

- (a) the physiologic balance of calcium metabolism;
- (b) the calcium intake by any given person from his self-selected diet;
- (c) the laboratory method used in arriving at reliable calcium content values of water; and

- (d) testing the hard water theory in animal experiments.

(a) Nicolaysen, 1972 [15] pointed out that the differences in the calcium content of water could maximally result in a daily extra intake of about 200 mg calcium in the hard water areas. "200 milligrams calcium added to a daily diet containing 500–800 mg of calcium will result in a flux of 10–20 mg through the human body per day. The level of calcium in the blood plasma is under a very fine control by several hormonal factors and it would have been advisable that experts in the field of calcium metabolism had been consulted before ill-founded hypotheses were suggested".

(b) The hardness of the municipal water supply as reported by public health departments does not insure that individuals *living in hard water areas* actually consume a higher calcium content in their average diet. In one pilot study to investigate this assumption [16], it was found that approximately half of the subjects drank softened or treated water at home! Participants in this study also were highly mobile and several reported drinking water or coffee in 6 or 7 different localities during the week. The authors presented detailed tables on calcium content of commonly used food items and concluded that "food, not water, was the major determinant of calcium and magnesium intakes.... We selected a field study to obtain a picture of the usual eating practices of a larger sample living in a hard water community... Other factors such as the use of home water softeners, place and kind of employment, and location of restaurants, may be as important as the reported water hardness".

If—as in this pilot study among hard water community residents—the contribution of water to the total mineral intakes averaged only 7% for calcium (and 12% for magnesium) the results obtained by Crawford *et al.* certainly would need extensive re-evaluation.

(c) In addition, laboratory methods analyzing the calcium content of water need to be standardized. The data for calcium in hard water as reported by Hankin *et al.* [16] were considerably less than the value reported by official sources in this California community. The California State Department of Public Health had sampled at a central distribution point and used oxalate precipitation and EDTA or permanganate titration. Hankin *et al.* obtained samples from kitchen taps, the actual endpoint for the consumer and used atomic absorption methods.

(d) Only a limited number of animal experiments have been carried out to test the hard-soft-water-theory, summarized by Püschner *et al.*, 1969 [17]. In their own study on young pigs kept under identical environmental conditions except for drinking water with the usual calcium content vs distilled water the authors

confirmed "the opinion of other investigators that the mineral content of the drinking water does not influence the formation of early arteriosclerotic lesions". Similar results were quoted from experiments in chicken and swine by different investigators in Germany and England.

WATER HARDNESS AND ASSOCIATED RISK FACTORS

Leaving these considerations aside, it is in order to more closely examine the 'explanation' in favor of the 'water story' as presented by the Crawford group in one of their latest publications, Stitt *et al.*, 1973 [18] on the subject:

"Observed differences, in the hard and soft water areas, in blood pressure and cholesterol could be important in explaining a substantial part of the difference in cardiovascular mortality between hard and soft water towns".

1. However, in the study by Elwood *et al.*, 1971 [19] in South Wales no differences were detected in cholesterol levels or blood pressures among men from two widely different areas in regard to water hardness ("hard water" meaning 250–270 ppm and 350–380 ppm in contrast to "soft water" 30–50 ppm)—Tables 1 and 2.

2. On the contrary, Bierenbaum *et al.*, 1973 [20] found the blood pressure levels higher in a "hard water" area than in the "soft water" area and the cholesterol levels likewise significantly higher in two areas in England (London) and the U.S.A. (Omaha) with *hard* water supply. However, in a second study (1975) by the same investigators [21], no differences in cholesterol levels were detected between hard and soft water areas in the U.S. (Twin Kansas Cities)—Tables 1 and 2.

3. Triglyceride levels [21] were unusually high in two studies in the United States, but without differences between "hard" and "soft" water areas. Only in England the triglyceride levels were found to be 14% higher in London (hard water) as in Glasgow (soft water)—Table 3.

It is obvious, then, that we can dismiss the notion of a 'water factor' operating via the common risk factor determinants. More relevant clinical measurements

TABLE 1. CONTRASTING RESULTS OF BLOOD PRESSURE LEVELS AS REPORTED FROM THREE STUDIES IN 'HARD' AND 'SOFT' WATER AREAS

Parameter examined	'Hard water' area	'Soft water' area	Significance	Authors
Casual BP	(N = 244 ♂)	(N = 245 ♂)		Stitt <i>et al.</i> , 1973
Systolic	137	139	n.s.	
Diastolic	84.7	87.5	P < 0.01	
Supine BP				
Systolic	139	142	n.s.	
Diastolic	85.5	87.6	P < 0.05	
BP	(N = 243 ♂)	(N = 357 ♂)		Elwood <i>et al.</i> , 1971
Systolic	140	138	n.s.	
Diastolic	87	85	n.s.	
BP	(N = 260 ♂ + ♀)	(N = 260 ♂ + ♀)		Bierenbaum <i>et al.</i> , 1975
Systolic	129	121	} P < 0.01	
Diastolic	83	78		

TABLE 2. CONTRASTING RESULTS OF CHOLESTEROL LEVELS AS REPORTED FROM FOUR STUDIES IN 'HARD' AND 'SOFT' WATER AREAS

Parameter examined	'Hard water' area	'Soft water' area	Significance	Authors
Cholesterol mg%	(N = 244 ♂)	(N = 245 ♂)		Stitt <i>et al.</i> , 1973
	237	245	$P < 0.05$	
	(N = 243 ♂)	(N = 357 ♂)		Elwood <i>et al.</i> , 1971
	220	223	n.s.	
	(N = 196 ♂ Omaha)	(N = 191 ♂ W.S.)*		Bierenbaum <i>et al.</i> , 1973
	241	228	$P < 0.05$	
	(N = 149 ♂ + ♀ London)	(N = 107 ♂ + ♀ Glasgow)		
	230	216	$P < 0.05$	
	(N = 260 ♂ + ♀)†	(N = 260 ♂ + ♀)‡		Bierenbaum <i>et al.</i> , 1975
	192	191	n.s.	

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†Kansas City, KS.

‡Kansas City, MO.

are needed to take the 'water story' seriously into consideration for preventive action. The proponents [18] believe they have discovered another difference which may account for the alleged mortality variations between hard and soft water areas, i.e. heart rate (higher in soft water than in hard water regions). This is a very crude measurement and clinicians would hardly accept a 78/min heart rate (soft water areas) vs 74/min heart rate (hard water areas) in spite of its statistically significant difference as proof of its biological significance. ECG measurements would be more appropriate and, here, another surprise was revealed by Elwood *et al.*, 1971 [19]: P-R interval was significantly longer in the men in the hard water area, and a 40-complex trace showed ventricular extra-systoles in a significantly higher proportion of these 243 men than in those 357 men in the soft water area (7 vs 2.8%). This latter finding is of considerable interest since the presence of ventricular extra-systoles in a routine ECG has been shown to indicate an increased mortality risk in long-term followup epidemiological studies. A Canadian study (Anderson *et al.*, 1969) [10] reported that a higher death rate in the soft water areas of Ontario "was found to be due entirely to an excess of sudden deaths. This finding suggests that the correlation between cardiac mortality and water hardness may be the result of an increased susceptibility to lethal

TABLE 3. TRIGLYCERIDE LEVELS IN 'HARD' AND 'SOFT' WATER AREAS

Parameter examined	'Hard water' area	'Soft water' area	Significance	Authors
Triglycerides mg%	(N = 196 ♂ Omaha)	(N = 191 ♂ W.S.)*		Bierenbaum <i>et al.</i> , 1973
	186	178	n.s.	
	(N = 149 ♂ + ♀ London)	(N = 107 ♂ + ♀ Glasgow)		
	137	120	$P < 0.05$	
	(N = 260 ♂ + ♀)†	(N = 260 ♂ + ♀)‡		Bierenbaum <i>et al.</i> , 1975
	198	191	n.s.	

*Winston-Salem, NC.

†Kansas City, KS.

‡Kansas City, MO.

arrhythmias among residents of soft water areas". The contribution from Elwood's clinical investigation would refute this assumption. Also, the Canadian study [10] has been criticized by Neri *et al.*, 1971 [22] after a careful review of the available data on sudden death in soft water areas of Ontario: "In the opinion of the present writers, the Ontario statistics so far examined, taken as a whole, hardly sustain Anderson's hypothesis....Our statistical analyses suggest that in Canada generally, water hardness does not have the value as a predictor of CHD mortality rates that it has been shown to have in the United States, England etc".

On the other hand, in the Elwood study [19], the clinical relevance of a slightly prolonged P-R duration (0.17 sec in hard and 0.16 sec soft water areas) is yet unknown. R-R and Q-T intervals were identical in both groups. In addition, answers to the Rose questionnaire produced a higher prevalence of angina in the hard water area (though not significant) which, again, is inconsistent with a lower cardiovascular mortality in the hard water region (Elwood *et al.*, 1971) [19]. The previously quoted study from the Twin Kansas Cities [21] presented significant differences in the percentages of abnormal electrocardiograms, i.e. 11.6% among 260 adults in the hard water area and only 4.2% among 260 matched persons in the soft water area ($P < 0.01$). "Coronary heart disease in the hard water area of Kansas City, KS is about 1.3 times that of Kansas City, MO where water from the same source is softened".

INTERNATIONAL STUDIES SHOWING NEGATIVE OR OPPOSITE RESULTS

Previous reviews of the subject have conspicuously requested from the same articles in favor of the 'water story' whereas publications at variance with the prevailing opinion were largely disregarded. In Holland, Biersteker, 1967 [23] and in Sweden, Bostrom and Wester, 1967 [24] reported that hard water was related to decreased cardiovascular mortality among women but not men. The opposite finding emerged from Newfoundland (Fodor *et al.*, 1973) [25]:

A death certificate study, examining the relationship between residence in the soft water area of St. John's and two communities with hard water supply with deaths from ischemic heart disease showed the following results: Whereas 441/100,000 men from the soft water area were listed as deaths due to ischemic heart disease, 327/100,000 men from hard water communities had this diagnosis on death certificates. *The age- and sex-adjusted data did not reveal any differences for females:* In both, the hard and soft water areas deaths due to ischemic heart disease were found in 150/100,000 females. The authors did not attempt to explain this sex difference and pleaded for "rigorously designed studies before valid conclusions can be reached". Mulcahy, 1964 [26] in Ireland found no relationship at all. Lindeman and Assenzo, 1964 [27] in their investigation of the relationship between water hardness and cardiovascular deaths in rural counties of Oklahoma (minimizing geographic and environmental variables) detected large variations among observed cardiovascular rates and also among levels of water hardness. They could not find significant correlations between water hardness and CHD. Masironi, 1973 [28] quoted a study conducted in Sardinia with likewise negative results. Already back in 1962, Davies [29] drew attention to this remarkable exception of the British studies—Birmingham, with its very soft water and low cardiovas-

cular mortality, similar to the neighbouring Midland county boroughs with their hard water supply and low cardiovascular death rate. Roberts and Lloyd, 1972 [11] found "it difficult to accept the hypothesis that hardness of water is causally associated with I.H.D. mortality when one million people (in Birmingham) who drink some of the softest water in England and Wales have the same low mortality experience from I.H.D. as half a million people, living less than 10 miles away, who drink some of the hardest water".

The International Atherosclerosis Project (Strong *et al.*, 1968) [30]—based on studies of 23,207 sets of coronary arteries and aortae submitted by pathologists from 14 countries—concluded: "These data show little association between water hardness and the prevalence and extent of atherosclerotic lesions in geographically different populations of autopsied cases. In addition, no convincing evidence of real association between water hardness and coronary artery stenosis was found.... The prevalence and extent of atherosclerotic lesions in 18 geographic and ethnic groups do not appear to be associated with water hardness or the concentration of common minerals. The results suggest that variations of water hardness do not materially contribute to the explanation of major differences in the extent of arterial atherosclerosis among cases from these different geographic locations".

Finally, Comstock, 1971 [31] studied the issue in Washington County, MD and found the risk associated with water hardness in the opposite direction from that reported in the original American-British studies. Fewer persons with soft water at home and more persons with hard water at home died from atherosclerotic heart disease than would have been expected from the distribution of controls. Comstock summarized: "A review of all the studies on water hardness shows that its correlations with cardiovascular disease are not often similar with respect to magnitude, to sex or age groups affected, or to the type of disease involved. These inconsistencies, taken together with the considerable number of heterogeneous noncardiovascular causes of death that are also related to water hardness, make it difficult to accept water hardness per se as anything but a spurious risk factor". Indeed, Lowe *et al.*, 1971 [32] found some evidence of an inverse relation between the frequency of malformations of the central nervous system and the hardness of the local water supplies, in the sense that hard water areas tend to have lower malformation rates than soft water areas. "It is concluded that the relationship between these associations may well be secondary". It is interesting to review an earlier paper by Crawford *et al.*, 1968 [33] in which *general* mortality rates were affected by the 'water factor', e.g. infant mortality as well as death from bronchitis and cardiovascular diseases were reportedly higher in soft water areas. Lately, however, these general mortality figures have not been re-examined, at least not reported in the recent literature. The question of causation vs association is once more raised.

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The Problem with Triglycerides

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One lay publication recently informed its readers that an elevated triglyceride (TG) level 'increases the chance for heart attacks markedly, regardless whether the cholesterol level is high or low. It appears indeed of importance to be concerned about one's TG levels and to disregard cholesterol levels'. Similar statements have proposed this attitude in connection with publications by Prof. Yudkin who, for over two decades, has defended (unsuccessfully) his hypothesis that sugar intake and ischemic heart disease (IHD) are more closely correlated than fat intake and the present epidemic of coronary heart disease (CHD). Yudkin's 'saccharine view' links the metabolic consequence of a high sugar intake — hypertriglyceridemia — with the increased incidence of ischemic heart disease.

The past decade was one of intensive research of the importance of hypertriglyceridemia as a risk factor in its own rights for the development of IHD. In the early sixties it appeared that serum TGs (upper normal levels for fasting TGs: 150 mg%) might be of equal or even greater value in the predictability than cholesterol levels. These assumptions were based on indirect estimation methods of TGs. Two prospective studies (*Albany and Framingham*) demonstrated that the predictability of TG is of less value than that of cholesterol (*Brown et al.*, 1965). Only 'in women over 50, prebetalipoprotein was superior to cholesterol in discriminating potential CHD cases. Risk of CHD in men can be estimated using any of the lipids; however, none proved more useful than an accurate total serum cholesterol' (*Kannel et al.*, 1971). The academic argument was revived in 1972 and 1973 by the results presented from the Stockholm study and therefore require some closer inspection. *Carlson and Böttiger* (1972) and *Böttiger and Carlson* (1973) assessed the role of serum TGs in the Stockholm prospective study with 71 men developing IHD within 9 years. Figure 1 'shows the rate of new events for persons below age 60, over age 60, and for all ages. The subjects in each decade have been grouped into quintiles according to their TG value,

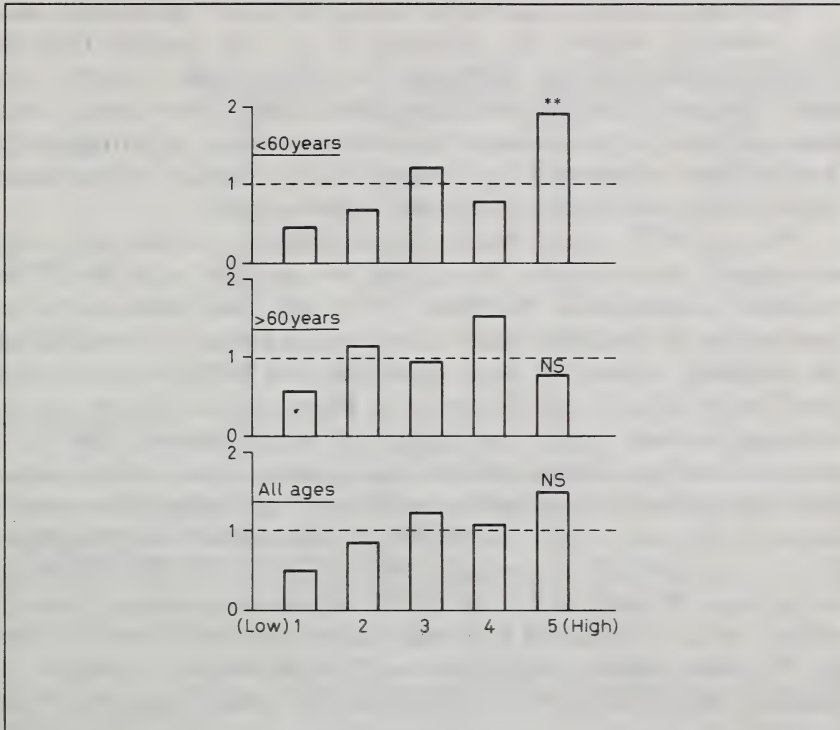


Fig. 1. Rate of new events of CHD in relation to initial plasma TG levels and age (Böttiger and Carlson, 1973).

quintile I thus comprising the subjects with the 20-percent lowest TG values, etc. The rate given is the incidence (number of new events divided by the number of individuals at risk) in each quintile, divided by the incidence rate of the whole population, i.e., the rate 1 (broken line) is that of the population. Statistical tests were performed to see whether the rate in the extreme quintile is different from the rate in the other four quintiles. Two asterisks indicate a significance level of $p < 0.01$.

Obviously, for men beyond age 60, and for all ages combined, initial TG values are of no predictive value in IHD. The men below age 60 show a trend of an increasing rate from the first to the third quintile. However, the rate of subjects in the fourth quintile is lower again, almost similar to the rate in the second quintile. There is no linear relationship between increasing TG levels and IHD rates. Neither from the 1972 nor 1973 publication is it possible to find out how many of the 71 men in this prospective study were in the below-age-60 group. How many men were actually in each quintile?

We do not know, and agree with *Stamler* (1973) that 'the published data do not necessarily warrant this inference. It is very possible that hyperprebetalipoproteinemia has significance for atherogenesis, — chiefly, perhaps solely — because of the associated hypercholesterolemia. No evidence is available indicating that — in the absence of hypercholesterolemia — hypertriglyceridemia (whether from endogenously synthesized VLDL molecules or from absorbed chylomicrons) is associated with intensified atherogenesis'.

Fidanza (1972) opined that the risk for IHD only increases with elevated, endogenously formed serum TGs *if* they are associated with elevated serum cholesterol concentrations. *Blackburn* (1974) went even further in his critical comments to the Stockholm study: 'These data on fasting TGs and CHD risk do not adequately account for serum cholesterol level in the crude and arbitrary cut-off values for each variable used in the simple analysis. The only significant prediction obtained was for cases having both serum cholesterol and TGs high, compared with those having both low. Age, glucose tolerance, blood pressure — all of which may be associated with TG levels and with CHD — were not accounted for, and at best the Stockholm information is only suggestive. ... There is the gradually accumulating evidence concerning the relationship of fasting serum TG levels to the risk of CHD in *general populations*. None of the evidence, so far accumulated in *general populations outside hospitals*, indicates that TG levels contribute information on CHD risk which is independent of the associated serum cholesterol level. Despite the clinical association between patients with atherosclerotic diseases and the mixed lipid phenotypes IIB, III and IV, the evidence so far in systematic follow-up of populations is that serum TGs, or the TG-rich lipoproteins, are relatively weak contributors to simple CHD-risk prediction and are essentially non-contributory after adjustment is made analytically for the associated serum cholesterol level.'

The Gothenberg data, in which other risk elements including serum cholesterol were adequately handled in the analysis, revealed no residual prognostic importance for fasting TG levels (*Wilhelmsen et al.*, 1973). Even one of the most active 'promoters' of TGs, *Albrink* (1973), had to admit that the prestigious Coronary Drug Project has found no independent contribution of TGs to future vascular disease. Further analysis of the Coronary Drug Project Research Group (1974) — basing their experience on a 3-year observation period including 2,789 men with sustained myocardial infarction — showed the following parameters of prognostic importance for the prediction of re-infarction or death from myocardial infarction: permanent ST segment depression in the resting ECG, cardiomegaly, New York Heart Association functional class, ventricular conduction defects, intermittent claudication, serum cholesterol, ventricular ectopic beats on the resting ECG and Q-wave abnormalities. It was specifically stated: 'While serum cholesterol was significantly related to risk of dying, serum TGs were not'. Our own study in Evans County, Ga. (*Heyden et al.*, 1972) compared

Table I. Age-adjusted TG levels in persons with and without IHD and stroke (Heyden *et al.*, 1972)

	White males mg%	White females mg%	Black males mg%	Black females mg%
With IHD	133 (59) ¹	117 (28)	77 (8)	108 (19)
Without IHD	127 (506)	126 (615)	95 (222)	99 (343)
With stroke	128 (26)	134 (8)	95 (9)	121 (11)
Without stroke	128 (539)	125 (635)	95 (221)	99 (351)

Differences in the TG levels between subjects with and without cardiovascular disease are not statistically significant by covariance analysis.

1 Figures in parenthesis = number of subjects.

Table II. Serum cholesterol concentrations (1960–62) and incidence per 1,000 of IHD (Tyroler *et al.*, 1971)

1960–62 cholesterol	Age	≤ 219 mg%	≥ 220 mg%
1967–69: IHD in men	35–44	59	66
	45–54	65	96
	55–64	122	148
	65–74	179	323
1967–69: IHD in women	45–54	29	30
	55–64	39	42
	65–74	59	178

retrospectively the TG levels in patients with IHD and patients with cerebrovascular disease with TG levels of persons remaining free of vascular disease – a total of 1,800 persons (table I); in all race-sex groups TG levels did not differ significantly from the TG levels obtained in healthy persons. On the other hand, cholesterol levels – in our own incidence study in Evans County, Ga. – showed the same high predictability for the development of IHD within a 7–8-year observation period as in many other epidemiological long-term studies (table II).

Conclusion

In contrast to the frequently stated opinion that hypertriglyceridemia carries a risk for the development of IHD *independent of associated hypercholesterolemia*, evidence so far is lacking. Convincing prove for the clinical relevance of an isolated TG elevation still remains to be presented by its proponents.

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2

Epidemiological Data on Dietary Fat Intake and Atherosclerosis with an Appendix on Possible Side Effects

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I. INTRODUCTION

Epidemiological data on the relationship between dietary fat consumption and atherosclerosis have been presented in thousands of articles in medical journals, hundreds of medical textbooks and several prospective long-term studies in the United States. In order to gain an

overall view of new developments in the field of research on hyperlipidaemia and clinical manifestations of atherosclerosis, it is necessary to discuss the hyperlipoproteinaemias first. However, since no prospective data are available on the relationship between specific types of hyperlipoproteinaemia and clinical manifestations of atherosclerosis, this chapter then discusses the well studied relationship of serum cholesterol concentration, dietary fat intake and the development of ischemic heart disease.

"Few controversies have divided the medical community so sharply for such a long time as has the sterol hypothesis. The separation between two points of view has become so extreme that, on the one hand, there are respected scientists who believe that the evidence is already so convincing that further clinical testing is unnecessary, financially wasteful and actually unethical; and, aligned against them, are equally respected scientists who believe that the total weight of evidence accumulated over the many years is too slight to justify further work along these lines. The opinion of one of these groups may very well be substantiated eventually. On the one hand, evidence in favor of the hypothesis is inadequate to persuade the medical profession to place itself solidly behind an attempt to lower the plasma cholesterol level of the general population. On the other hand, the evidence is sufficiently suggestive to prevent the scientific community from discarding the hypothesis. In fact, a large share (probably more than half) of the research now in progress in the field of atherosclerosis is concerned with some aspect of the hypothesis." (Frantz and Moore, 1969.)

Later in the chapter the subject of dietary intervention is divided into two categories: primary prevention of ischemic heart disease (Section VII) where four internationally known trials will be covered and secondary prevention in patients with ischemic heart disease (Section VIII) where seven studies from several countries will be presented first, followed by four trials conducted in England with negative results.

II. HYPERLIPOPROTEINAEMIA AND ATHEROSCLEROSIS

Only two manifestations of atherosclerosis have been associated with specific types of hyperlipoproteinaemia: coronary heart disease and peripheral vascular disease. There is no report to date of a relationship between cerebral vascular disease and any type of hyperlipoproteinaemia; however, a negative association between cerebrovascular disease and hypercholesterolaemia has been reported in several long-term prospective studies.

The hyperlipoproteinaemias can be classified in different types, (Fredrickson *et al.*, 1967) of which, type II, type III and type IV have been associated with atherosclerosis and its manifestations in several retrospective studies. In patients with the very uncommon type I syndrome no manifestations of coronary artery disease have been found. Type V patterns are also rare, and evidence of accelerated atherosclerosis in either patients or their families has not been striking.

Table 1

Hyperlipoproteinaemia in recent studies of patients with ischemic heart disease, and controls

		Per cent distribution of hyperlipoproteinaemia				
No. of patients with IHD		Normal	II	III	IV	V
(5 studies)						
126	Boston/Bethesda ^a	46	29	0	25	0
70	Buffalo, N.Y. ^b	26	44	0	30	0
108	Aalborg, Denmark ^c	22	43	11	16	8
105	Drammen, Norway ^d	43	31	0	26	0
100	Göteborg, Sweden ^e	41	24	13	22	0
Average		36%	34%	(5%)	24%	—
		Per cent distribution of hyperlipoproteinaemia				
No. of "normal" persons		Normal	II	III	IV	V
(4 studies)						
66	Boston/Bethesda ^a	89	3	0	8	0
11	Buffalo, N.Y. ^b	64	18	0	18	0
109	Aalborg, Denmark ^c	78	7	4	10	1
76	Göteborg, Sweden ^e	75	12	1	9	3
Average		77%	10%	(1%)	11%	(1%)

^a Heinle *et al.* (1969).

^b Falsetti *et al.* (1970).

^c Dyerberg *et al.* (1970).

^d Enger and Ritland (1970).

^e Werkö (1971).

Prevalence of hyperlipoproteinaemia in the general population was estimated by one author to amount to only 5% of Americans (Connor, 1970). More precise estimates will be forthcoming from the present Hyperlipoproteinaemia Prevalence Study, conducted by the National Heart and Lung Institute (NHLI). Preliminary analysis of available data would place this percentage considerably higher. Table 1 shows the per cent distribution of the hyperlipoproteinaemias in different parts of the United States and Scandinavia among patients with ischemic heart disease (IHD) and among those believed to be free of it.

More than one-third of patients with ischemic heart disease had a normal lipid electrophoresis according to these investigations published in 1969, 1970 and 1971. As expected, the most frequently observed type of hyperlipoproteinaemia in patients with ischemic heart disease was type II (34% of all patients), followed by hyperlipoproteinaemia type IV (24% of all patients). Since in some instances the "control population" was selected from hospitalized patients (with illnesses other than ischemic heart disease), the per cent distribution of hyperlipoproteinaemias in these populations are not indicative of the prevalence of hyperlipoproteinaemias in the general population. But it is interesting that 77% of all subjects without ischemic heart disease were found to have a normal electrophoresis, only 10% showed hyperlipoproteinaemia type II and 11% hyperlipoproteinaemia type IV. Prospective data concerning the risk of ischemic heart disease or peripheral vascular disease in relation to lipoprotein types are non-existent.

Type II

Hyper- β -lipoproteinaemia studied by Slack (1969) in male patients was associated with a mean age (at onset of ischemic heart disease) of 43 years and among female patients of 48 years. In the study by Jensen *et al.* (1967) the mean age at death from coronary disease in men with hyperlipoproteinaemia type II was 56 years, and the mean age at death in women was 58 years. The age at onset of, and age at death from, ischemic heart disease therefore is clearly much younger than the average age of onset and mean age of death from ischemic heart disease in the general population, when not associated with hyperlipoproteinaemia II.

Arteriosclerotic-type plaques have been observed in major pulmonary arteries in type II patients who have had no evidence of pulmonary hypertension. In addition, Roberts *et al.* (1970) described a peculiar valvular disease in five patients with hyperlipoproteinaemia II. The finding of extensive plaquing in the ascending aorta and proximal coronary artery in these young subjects who had no histories of rheumatic

or congenital cardiac disease suggests an atherosclerotic etiology of the valvular disease. The finding of cholesterol clefts and foam cells in the aortic valve cusps is also strongly suggestive of an unusual etiology of valvular heart disease, namely atherosclerosis.

A surprisingly low frequency of peripheral atherosclerosis associated with familial hypercholesterolaemia (type II) was found by Harlan *et al.* (1966).

“Two explanations may be offered. Arterial disease may develop early and follow a constantly progressive course which initiates parallel development of collaterals and minimizes the effect of arteriosclerotic narrowing. Alternatively, hypercholesterolaemia is not associated with a severe arteriosclerotic process in the peripheral arteries. The fact that arteriosclerosis obliterans is more frequently associated with abnormal glucose tolerance than hypercholesterolaemia is consistent with this last hypothesis. Glucose tolerance was normal in familial hypercholesterolaemia.”

Widmer *et al.* (1969) were surprised not to find any difference in cholesterol levels and specifically hypercholesterolaemia among patients with peripheral atherosclerotic disease and healthy persons. The frequency of hypercholesterolaemia in patients with intermittent claudication was 20.5%, and the frequency of hypercholesterolaemia among the healthy persons without intermittent claudication was 16%. However, β -lipoprotein concentration was found significantly higher among the patients than among the healthy persons. Thirty-nine per cent of patients with intermittent claudication had elevated β -lipoproteins, whereas only 17.5% of the healthy persons had elevated β -lipoprotein levels. Unfortunately pre- β -lipoproteins were not measured. This finding is most unusual and contrary to several other investigations, the most recent one by Greenhalgh *et al.* (1971). Only 5% of their patients with peripheral vascular disease had hyper- β -lipoproteinaemia, whereas 30% had hypertriglyceridaemia with normal cholesterol levels. Electrophoresis, in most cases, showed increased pre- β -lipoprotein levels.

Type III

“Occlusive vascular disease is a serious and frequent accompaniment of type III. In the samples observed by us, occlusive peripheral vascular disease, especially of femoral and popliteal vessels with severe claudication, has been at least as frequent as coronary atherosclerosis.” (Fredrickson *et al.*, 1967.)

Slack reported that in men with types III, IV and V hyperlipoproteinemia, the risks were lower for ischemic heart disease than with type II,

but the risk of peripheral vascular disease was increased. In his study the age of onset of ischemic heart disease seemed to be later in both men and women with types III, IV and V hyperlipoproteinaemia than with type II. There was also a notable absence of death from ischemic heart disease among patients with hyperlipidaemia associated with hypertriglyceridaemia. He concluded

"The absence of deaths and the incidence of peripheral vascular disease among patients with types III, IV and V hyperlipoproteinaemia, suggests that there may be a real difference in the type of atheromatous lesion which develops compared with the more lethal disorder of type II hyperlipoproteinaemia."

In a detailed study of the peripheral circulation (Zelis *et al.*, 1970) nine out of twelve patients with hyperlipoproteinaemia type III showed subnormal values of the peak reactive hyperaemia blood flow. No significant differences in the peak reactive hyperaemia blood flow were demonstrable in patients with type II or type IV disorder in comparison to control persons.

Through combined use of drug and dietary treatment, patients with type III disease were considerably improved. The authors concluded that the "vascular cholesterol" in type III patients may be very labile. Combination therapy may have afforded a significant resorption of atherosclerotic plaques followed by increase of the arterial lumen with subsequent improved blood circulation.

According to Roberts *et al.* (1970) patients with type III are particularly susceptible to the development of peripheral arterial disease,

"and objective improvement in peripheral blood flow also can occur with this medical regime."

Greenhalgh *et al.* (1971) suggested

"that increased pre- β -lipoprotein levels might predispose to atherosclerosis with a predilection for arteries supplying the lower limbs, is an intriguing possibility."

Type IV

"Premature coronary arterial narrowing frequently occurs . . . over 40% have hyperuricaemia." (Roberts *et al.*, 1970.)

Levy and Fredrickson (1970) emphasized the accelerated coronary vessel disease in type IV patients. Fredrickson *et al.* (1967) pointed out that in patients with the primary form of hyperlipoproteinaemia IV,

excessive body weight and abnormal glucose tolerance are extremely common. In their experience, the incidence of abnormal glucose tolerance in those with familial type IV patterns exceeded 90%. In a later study by the same group (Heinle *et al.*, 1969), 70% of patients with a type IV electrophoretic pattern demonstrated abnormal glucose tolerance. Schreibman *et al.* (1969) warned that the frequent finding of type IV hyper-pre- β -lipoproteinaemia in retrospective studies of patients selected because of coronary artery disease should not be interpreted as a possible risk of this lipid disorder. The risk may not be severe if obesity and diabetes mellitus do not co-exist even when onset of hyperlipoproteinaemia occurred in childhood.

"A careful screening for this disorder in the pediatric group may furnish the material for a prospective study large enough to define this possibility further."

A. Is Lipoprotein Electrophoresis Necessary?

Two answers are available to this question, one methodological, one epidemiological. According to the study by Schatz (1969) lipoprotein electrophoresis was not necessary for the identification of any of the 75 patients with type II and most (67 out of 71) patients with type IV hyperlipoproteinaemia. These two groups represent a majority (68.2%) of patients in his series. In only half of the twelve patients with phenotype III was the identification possible without electrophoresis. The very rare phenotype V could not be diagnosed without lipoprotein electrophoresis. In this particular series, none of the twelve patients with previously classified V pattern could be placed into this category. However, the detection of a wide chylomicron band on paper electrophoresis could be replaced by the simple observation of the plasma after keeping it overnight in the cold. In this situation, chylomicrons appear as a cream layer at the top. Schatz, therefore, concluded that

"lipoprotein electrophoresis is not necessary for the proper identification of most patients with types II and IV hyperlipoproteinaemia, but may be of some benefit in separating patients with type III disease."

Harlan (1969) criticized that the lipoprotein electrophoretogram is a qualitative rather than a quantitative assessment, and, therefore, does not lend itself to quantifying the differences between individuals or the changes induced by therapy. In contrast, he writes,

"measurements of cholesterol and triglyceride are quantitative, more readily available and usually furnish sufficient information to type the hyperlipidaemia."

The second answer represents the epidemiological viewpoint. Kannel *et al.* (1971) reported on the risk of coronary heart disease over 14 years in Framingham where β -lipoprotein, pre- β -lipoprotein and cholesterol levels were examined in 2282 men and 2845 women.

"The mean level of each of the major serum lipids and lipoproteins was higher at the initial examination in those who went on to develop coronary heart disease than in cohorts who remained free of clinical manifestations of the disease over the 14-year period of observation. The risk for the development of coronary heart disease was proportional to the concentration of each lipid. The risk of ischemic heart disease proved proportional to the antecedent serum cholesterol level in men of all ages studied. Even after excluding persons with hypertension, diabetes, ECG abnormalities and the cigarette habit, a distinct gradient of risk proportional to the cholesterol concentration can be demonstrated. This tends to brand the lipid, not associated variables as the culprit . . ."

"When risk of coronary heart disease was examined according to pre- β -lipoprotein concentration, adjusting for cholesterol, no residual risk gradient remained in men and younger women. In women over 50 years of age, however, pre- β -lipoprotein was superior to cholesterol levels in discriminating potential coronary heart disease cases."

Kannel *et al.* therefore concluded that in men

"knowledge of the serum lipoprotein levels and the cholesterol concentration appears to provide no better discrimination of potential coronary victims than can be deduced from an accurate serum cholesterol value alone. Any one of the lipids or lipoproteins examined and by inference, a triglyceride as well can be used effectively for assessing vulnerability to coronary heart disease. None, however, would appear superior to the more convenient cholesterol determination for this purpose. In women, the picture appears to be somewhat different. In women under the age of 50, as in men, high cholesterol values and not pre- β -lipoprotein appeared to be associated with an increased risk. In older women, on the other hand, cholesterol appears to have no predictive value, and pre- β -lipoprotein actually appears to be superior to cholesterol for estimating."

The excellent predictability of an elevated cholesterol level for the development of myocardial infarction has been demonstrated in several long-term epidemiologic prospective studies, among others in our own Evans County Study (1971). We found over an eight- to nine-year observation period that for men with cholesterol levels of 260 mg % and above, the risk of developing ischemic heart disease was twice as high as

for men with cholesterol levels below 220 mg %. Similarly, an excellent agreement between levels of serum cholesterol and significant arterial lesions observed in coronary angiography was found by Welch *et al.* (1970). Among 169 men with cholesterol levels less than 200 mg %, only 20 % had significant lesions. Among 186 men with levels more than 275 mg %, 81 % had significant lesions. There was a gradual increase in the percentage of significant lesions for each serum cholesterol level concentration, reaching almost 100 % in those men with cholesterol levels above 350 mg %. It is noteworthy that all men examined were under 40 years of age.

From the therapeutic standpoint, it should be recalled that over the past 15 years all dietary studies as means of primary prevention of ischemic heart disease or in the secondary prevention of reinfarction, concentrated on and were directed towards lowering of cholesterol levels. Although almost none of these studies were conducted in a double blind fashion with strictly comparable control persons, the trends in the results of both primary and secondary prevention studies seemed to favour the effect of a diet low in cholesterol and relatively high in polyunsaturated fatty acid to prevent ischemic heart disease and reinfarction. The conclusion, therefore, is justified that the measurement of the serum cholesterol concentration in an attempt to assess the risk of a man or woman (below the age of 50) for the development of ischemic heart disease as well as the treatment of hypercholesterolaemia would contribute significantly to the early detection and prevention of this epidemic disease. Additional assessment of the triglyceride levels would certainly be of help since a different dietary approach is indicated, and this might be a valuable contribution in the prevention of ischemic heart disease particularly in women above age 50, according to the Framingham data. The relative ease with which dietary changes produce complete normalization of abnormal hyperlipoprotein patterns (III, IV) and serum cholesterol as well as serum triglyceride concentrations should be encouraging to practising physicians. One cannot but be impressed by the fact that an appropriate dietary management of a cooperative and motivated patient can in most cases take the place of drug therapy. Notable exceptions to this statement are type I and IIa.

The importance of dietary influences on hyperlipoproteinaemias was demonstrated again by the study of plasma lipid and lipoprotein pattern in Greenlandic West Coast Eskimos (Bang *et al.*, 1971). The food of this population is very rich in protein, the quantity of carbohydrates is extremely small (estimated to be only 54 g per day) and a high animal fat intake of sea animals containing a large amount of polyunsaturated fatty acids. The levels of serum cholesterol and triglycerides as well as

serum β -lipoprotein and pre- β -lipoprotein were substantially higher in Danish controls than in the Greenlandic Eskimos. A most striking observation was the near absence of pre- β -lipoproteins on the electrophoretic strips. Both plasma cholesterol and β -lipoprotein concentrations were at a very low level. The level of these lipids did not increase with advancing age—as was the case in Danish males. The low lipid levels were associated with a very low incidence of ischemic heart disease and with a near absence of any case of diabetes mellitus.

B. Progress Report on Lipoprotein Phenotyping 1973

In 1954 the technical group of a Commission on "Lipoproteins and Atherosclerosis" came to the conclusion that the measurement of lipoprotein-concentrations is not superior to the simple measurement of serum cholesterol levels in its predictive power for ischemic heart disease. Almost 20 years later, a new trend seems to have evolved postulating that the measurement of cholesterol and triglyceride concentrations in the serum may be sufficient to give a valuable prediction for ischemic heart disease. Lipoprotein electrophoresis, according to some investigators, may not improve the predictive power of the combined measurement of cholesterol and triglycerides (Kannel *et al.*, 1971; Stamler, 1973). During almost two decades between these two statements lipoprotein electrophoresis has received wide attention although this typing system has undergone some criticism.

Pries *et al.* (1968) demonstrated the questionable reproducibility of the lipoprotein electrophoresis. Several investigators reported on intra-individual changes of types in multiple determinations which were hard to explain, e.g. type V converting into type IV under caloric restriction (Brunzell *et al.*, 1971); type V may convert temporarily into type II before complete normalization under isocaloric carbohydrate-reduced diet (personal observation, unpublished); type IV patients may convert under drug treatment with Atromid in some cases into type II (Strisower *et al.*, 1970). Hazzard *et al.* (1973) reported that

"in many instances a small quantitative change in the level of either LDL-cholesterol or whole plasma triglyceride caused qualitative differences in lipoprotein phenotypes, especially in individuals with familiar combined hyperlipidaemia, who showed variable expression (types IIa, IIb, IV or V)."

These investigators examined the relationship between lipoprotein phenotypes and genetic lipid disorders in 156 genetically defined survivors of myocardial infarction. The lipoprotein phenotype of each

survivor was determined primarily by measurement of his plasma triglyceride and low density lipoprotein (LDL)-cholesterol concentrations; his genetic disorder was identified by analysis of whole plasma cholesterol and triglyceride levels in relatives.

"On an individual basis no lipoprotein pattern proved to be specific for any particular genetic lipid disorder; conversely, no genetic disorder was specified by a single lipoprotein pattern."

These drawbacks in the interpretation of the results of the lipoprotein electrophoresis make it difficult at the present time to find a classification of lipid abnormalities which would satisfy everybody. The latest (although certainly not last) suggestion comes from the Seattle Group (University of Washington), Goldstein *et al.* (1973), differentiating five distinct lipid disorders.

1. *Familial Hypercholesterolaemia*

This was characterized by the finding of pathological cholesterol levels in relatives of patients with myocardial infarction—all relatives had normal triglyceride levels. The cholesterol distribution was found to be bimodal and segregation analysis suggested autosomal dominant inheritance. The criterion which distinguished this disorder from other familial hyperlipidaemias was the nearly complete expression of hypercholesterolaemia in affected children.

2. *Familial Hypertriglyceridaemia*

This was characterized by the occurrence, in relatives of patients with myocardial infarction, of a normal cholesterol distribution but apparently bimodal triglyceride distribution. Segregation analysis in siblings again was consistent with autosomal dominant inheritance; however, hypertriglyceridaemia was not completely expressed in affected children (the study of offspring of affected subjects revealed that hypertriglyceridaemia was only expressed in about 13% of young relatives at risk).

3. *Familial Combined Hyperlipidaemia*

This was characterized by variability in expression of lipid levels among affected relatives of patients with myocardial infarction. Any combination of elevation in LDL-cholesterol and very low density lipoprotein (VLDL)-triglyceride or both, were observed among affected relatives. Affected individuals with this disorder manifested any one of four lipoprotein phenotypes: type IIa, IIb, IV or V patterns.

Dr Carlson commented at the 3rd Atherosclerosis Symposium in Berlin (October 24–28, 1973)

“IIb or not IIb—that is here the question, a direct quotation from Shakespeare.”

Dr Fredrickson (personal communication, 1973) said the

“great issue in the wind now is that of type IIb or combined hyperlipidaemia representing a muddle of confusion which will have to be clarified before the value of having a fairly precise measure of LDL can be determined.”

Nikkila and Aro (in Goldstein, 1973) independently reported that the most common form of familial hyperlipidaemia in survivors of myocardial infarction is one in which multiple lipoprotein types are observed among about 50 % of the first-degree relatives. These observations thus confirm the hypothesis by Goldstein *et al.*

4. *Polygenic Hypercholesterolaemia*

Neither hereditary nor identifiable environmental factors could be implicated. This disorder affected about 6 % of survivors.

5. *Sporadic Hypertriglyceridaemia*

Inheritance factors did not play a direct role in the pathogenesis of hyperlipidaemia in the survivors. The authors therefore designated them as “sporadic” cases in the non-genetic sense.

In October 1973, one of the original designers of the method for separating lipoproteins by electrophoresis, Dr Lees, summarized the present situation with the words

“The qualitative lipoprotein methods of ten years ago have served us well and are still of value. However, it is increasingly apparent that classification schemes based on these methods do not fully describe the clinical and genetic spectrum of the hyperlipidaemias. It is now time to perfect the quantitative techniques mentioned above, and to develop new ones, so that we can define phenotypes that reflect more accurately the inherited biochemical defects that underlie the primary hyperlipidaemias.”

Lees offered the following new classification

“This table serves as a convenient means of display of the available data, and hopefully, as a guide, during the confusing period in which old concepts are breaking down and new ones are being formulated.”

Present status of lipoprotein phenotyping

Present nomenclature	Fredrickson-Lees phenotype	Plasma concentration of			Presumptive kinetic defect
		Cholesterol	Glycerides	LDL protein	
Familial fat-induced lipaemia	I	Normal or high	Very high	Low	Impaired chylomicron removal
Familial hypercholesterolaemia	II (IIa, IIb)	High	Normal or high	High	Impaired β -lipoprotein removal
Broad- β -disease	III	High	High	Normal	Faulty conversion of pre- β to β -lipoproteins
Combined hyperlipidaemia	II, IIb or IV	Normal or high	Normal or high	Unknown	Unknown
Familial hyperglyceridaemia	IV	Normal	High	Normal	Impaired pre- β -lipoprotein removal
Mixed hyperlipaemia	V	High	High	Normal	Impaired removal of chylomicrons and pre- β -lipoproteins

III. SEASONAL CHANGES IN SERUM CHOLESTEROL CONCENTRATIONS

A discussion of epidemiological data on the relationship between dietary fat consumption and influences on serum cholesterol would, of course, be incomplete if seasonal changes were not mentioned.

In the report of the National Diet-Heart Study (1968) it was stated that

“there have been suggestions in the literature that serum cholesterol concentrations may show seasonal changes, with values in the winter being somewhat higher than in the summer. This would parallel the common finding that people gain weight during the winter and lose it in summer and could possibly be related thereto.”

However, the results were rather inconclusive. Analysis of the data

“does not prove that there is no significant seasonal trend in serum cholesterol, whether this be related to seasonal change in diet or to any other factor—for example endocrine changes. It does show that any possible seasonal effect does not greatly disturb the comparison between baseline values and average values for the whole period on prescribed diet.”

Our own experience in this regard is quite different and we feel that there is indeed a powerful seasonal influence on cholesterol levels which may present a major difficulty in the analysis of data from persons placed on diets. In our Hypertension Intervention Study in overweight, hypertensive individuals (Heyden *et al.*, 1973b) in Evans County, Georgia, 63 persons were placed on a low-sodium weight reduction programme and 64 persons who were not given dietary advice, were

charted for blood pressure measurements regularly. The baseline examination was done in August of 1971 during the peak of the heat and humidity characteristic for the summer season in Georgia. Cholesterol levels were comparable in both groups—mean level 211 mg% in the experimental and 212 mg% in the control group. Repeat cholesterol determination was done five months later during an unusual cold wave in January 1972, after an average weight loss of 8.0 kg (17.5 lb) in the experimental group and only 2.27 kg (5 lb) in the control group. It revealed a definite increase in cholesterol levels of an average 32 mg% in the experimental and an average of 35 mg% in the control group. In the experimental group, 38% remained at the baseline level ± 20 mg% but 58% increased in serum cholesterol concentrations more than 20 mg%. In the control group, 29% remained at their initial cholesterol levels ± 20 mg% but 69% increased more than 20 mg%. It is remarkable that in this obese, hypertensive population regardless of weight stability or weight loss after profound dietary changes, a definite increase in cholesterol levels was observed and that only two persons in the experimental group and only one person in the control group had decreased cholesterol levels by more than 20 mg% in five months.

Massek *et al.* (1962) reported important seasonal variations in cholesterol levels

“with a marked drop in summer and autumn . . . based on extensive epidemiological investigations, comprising all age groups from newborn infants up to people above the age of 80 years . . . in the Czech population.”

Chapman and Massey (1964) found that the highest mean values in the Los Angeles Heart Study occurred among persons examined in January and February; the lowest among August and September examinees.

Doyle *et al.* (1965) followed 52 men over a 12-month period.

“Almost 50% of the group had a maximum difference of at least 50 mg%. No person had a difference of less than 20 mg% and two had differences in excess of 100 mg%.”

The lowest levels were reached in July, while two peaks occurred in October/November and January/February.

Thorp (1963) emphasized that the amplitude and frequency of this variation differs according to location of the study and with the occupation, age and diet of the subjects studied.

“If the annual variation of serum cholesterol of individuals is examined, a great majority show two peaks, which generally occur in the spring and autumn . . . 65% of the seasonal patterns are

dicyclic, and only 28% monocyclic. Yet when the results are averaged the predominant impression is of a monocyclic pattern, with a maximum in winter and a minimum in summer."

Data presented by Paul *et al.* (1963) showed a consistent seasonal variation in cholesterol levels in 2107 middle-aged men. The highest serum-cholesterol concentrations were encountered during the winter, the lowest in the spring or summer. In four consecutive years (1958-61) the values obtained in the autumn were definitely higher than those in spring or summer but never reached the peak values of winter time. The cholesterol determinations were not made per man per season. The procedure was, rather, to use the data procured from annual examinations to find the mean for each season. The magnitude of the variations (10-30 mg% from the lowest to the highest difference) has previously been assessed by others, e.g. by Thomas *et al.* (1961) in 25 prisoners during monthly determinations for one year. Higher cholesterol levels tended to prevail in December of 1958 and in January and November 1959; lower values were more prevalent in warmer months. A sharp decline was seen from March to May, when the lowest point of the year was reached.

Thomas observed differences up to 50 mg% in the mean values of 16 young men, similarly to Doyle's report. Physical activity did not seem to be of any importance in lowering the cholesterol levels in the warmer season, since only a few prisoners took advantage of the opportunity of some increased outdoor activity. Thomas has collected information from the literature pertaining to this problem of seasonal changes and found conflicting reports, among others one from Japan, showing seasonal variations in activity of the thyroid gland with highest BMR in winter and lowest in summer.

The following section is a summary statement on the potential influence of weight reduction on cholesterol metabolism. By the nature of a reducing diet, fat intake is usually drastically reduced except in the so-called high-protein diets promoted by Dr Stillman and Dr Atkin which practically eliminate carbohydrate intake. My own findings with several obese patients on a fat-restricted diet (25 g fat, 60 g carbohydrates, 60 g protein) providing roughly 700 kCal per day will follow (see pp. 68-69).

IV. CHANGES OF CHOLESTEROL LEVELS DURING ACTIVE WEIGHT REDUCTION

Moses (1963) reported that a substantial drop in cholesterol occurs with weight loss followed after a few months at this weight level by a gradual

return to control values in almost all subjects. Bierenbaum *et al.* (1963) on the other hand, found a permanent reduction of the cholesterol level in weight-reducing men. Galbraith *et al.* (1966) reviewed the confusing and conflicting reports on this problem in the literature. However, three possible trends for cholesterol levels following weight reduction seem to emerge—a decrease (five reports), no change (three reports), an increase (two reports). In the study by Galbraith *et al.* of nine very obese people, a drastic average decrease of 54 mg% (from a normal baseline of 198 mg%) after the first three weeks of active weight reduction was followed by a subsequent increase in every individual. Unfortunately, this was designed as a short-term experiment and long-term results from obese patients have been rarely reported in the literature.

This last experiment is mentioned because of the perhaps surprising observation that the nine excessively obese subjects with an average weight of 158 kg (348 lb) had normal cholesterol levels. Hartmann (1965) commented that “extreme obesity (overweight by 50% or more) is mostly accompanied by relatively low serum lipids”. Connor and Connor (1972) wrote that physicians are often surprised that the heavy overweight subjects (135–270 kg: 300–600 lb) show a low cholesterol level (140–160 mg%). However, this was frequently seen in their practice in Iowa.

A typical example was the heaviest man ever seen in my clinic, a 36-year-old weighing 273 kg (601 lb). Both he and his friend, a 56-year-old man weighing 174 kg (384 lb), had cholesterol levels below 180 mg% on repeat examinations.

The National Diet-Heart Study (1968) reported a different finding

“There is a tendency for hypercholesterolaemia to be more common as relative weight increases and the relationship appears to be approximately linear on the relative weight decile scale. Roughly, the 10% of participants with highest relative weights were grossly hypercholesterolaemic about twice as frequently as the 10% men with the lowest relative weight.”

It may very well be that the National Diet-Heart Study was not concerned with grossly obese persons such as one is most likely to encounter in a special obesity clinic. In the experience of Van Houste and Kesteloot (1971) “cholesterol increases with weight up to 100 kg, but decreases at higher weight” in an epidemiological cardiovascular study of 42,804 military subjects. Schreibman *et al.* (1971) and Nestel *et al.* (1973) concluded from metabolic ward observations of eight obese patients that obese patients may double their cholesterol synthesis rate and cholesterol storage depot without increasing plasma cholesterol content: “In spite

of increased synthesis and increased body cholesterol content, plasma cholesterol is not elevated". These authors found a rise in plasma cholesterol specific activity following weight reduction. This observation was consistent in all "labelled" patients even though plasma cholesterol itself sometimes rose and sometimes fell (personal communication, Schreiberman, 1972).

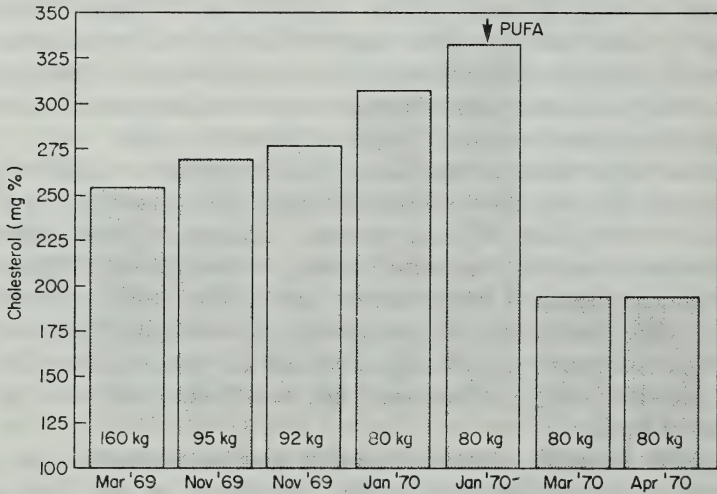


Fig. 1. Result of drastic weight reduction on cholesterol levels.

Figure 1 demonstrates the result of weight reduction on cholesterol levels in a 41-year-old man. He reduced his weight from 160 kg (352 lb), 3/1/69, to 80 kg (176 lb) by 12/31/69 (10 months) while continuing his profession as paint salesman without hospitalization and without any drug therapy to suppress his appetite. The cholesterol increased from 255 mg% at the beginning of his weight reduction programme to 335 mg% by the time he had reached his maintenance weight of 80 kg (176 lb) in January 1970. At this point we urged the patient to use polyunsaturated fat in the form of margarine for frying purposes and corn oil to be used in salads. By March 1970, the cholesterol had decreased predictably to 185 mg% and remained at this level during the following months. The remarkable fall of the cholesterol level can not simply be explained by the addition of polyunsaturated fatty acids to his diet. At the same time, between January and March, a seasonal effect has to be taken into account. The previous increase of the cholesterol level during active weight reduction in this patient is representative for a number of excessively obese persons; however, another reaction has been observed just as frequently.

In the past few years, we have seen many patients who were concerned about their slightly elevated cholesterol levels and who were disappointed

to find out that in spite of drastic weight reduction, the cholesterol level did not change at all.

In moderately obese subjects, weight reduction more often seems to cause a drop in cholesterol, in our present experience at least, more frequently than an increase in cholesterol levels. The lability of vascular cholesterol in hyperlipoproteinaemia type III is well known. It is, therefore, not surprising that patients with this lipid disorder always, without exception, show a large decrease in cholesterol levels during weight reduction.

It is obvious that these so far unpredictable changes in cholesterol levels during and after weight reduction must be studied more systematically, classifying obese persons in "mild", "moderate" and "excessive" cases, analysing the data separately by sex and by age.

V. CHANGES IN LIPOPROTEIN ELECTROPHORETIC PATTERN IN TYPES IV AND V DISORDERS WITHOUT AND/OR DURING WEIGHT REDUCTION

Strisower *et al.* (1970) suggested that

"in type IV disease, the effect of Atromid-S should be monitored with serial paper electrophoretic strips to allow a careful comparison of the intensity of the beta band. If the intensity of this band increases, an undesirable lipoprotein shift has taken place and Atromid-S should be stopped. Ultracentrifugal studies have shown that severe forms of type IV disorders frequently respond to Atromid-S with a marked increase in the beta lipoprotein concentration; this may be considered equivalent to the iatrogenic conversion of a type IV to a type II disorder. Since type II disorders are the most malignant disturbances in terms of association with severe coronary atherosclerosis, the substitution of a type II disorder disturbance for a type IV disorder is most likely deleterious to the patient. The type IV to type II lipoprotein shift is generally unimportant if the type IV disturbance is mild or moderate; if it is severe, a significant shift occurs in nearly all cases."

We have in our files a case of a conversion into type II pattern in a patient with previous type IV pattern.

J.F.M., a 42-year-old self-employed feed mill farmer presented himself on 7/9/71 for diet counselling weighing 149 kg (328 lb). (Aged 17 his weight had been 100 kg: 220 lb.) The 12-hr fasting serum was cloudy, cholesterol level was 320 mg%, triglyceride level 615 mg%, β -lipoproteins slightly increased, pre- β -lipoproteins increased. This was diagnosed as consistent with phenotype IV. The patient was placed on a strict weight reduction programme with

frequent intermittent fasting days. After nine weeks, his weight was reduced to 131 kg (289 lb) a weight loss of 18 kg (40 lb). He had worked continuously during this time and reported feeling well. His blood pressure had dropped from 180/125 mmHg to 110/88 mmHg. Lipid electrophoresis on 9/16/71 revealed the serum to be clear. Cholesterol had increased to 442 mg% while the triglycerides had markedly decreased to 252 mg%. β -Lipoprotein which was only slightly increased in the previous lipoprotein analysis was this time reported increased and pre- β -lipoprotein was, again, increased. The data were consistent with phenotype II. It is possible to explain this remarkable shift by the changes which took place in his thyroid function. On the day of his first lipid electrophoresis the thyroid-function tests, T3 and T4 as well as free thyroxine were reported to be at a low normal level. After hyperlipoproteinaemia type IV had cleared under weight reduction, he became increasingly myxedematous and the hyperlipoproteinaemia changed to type II. After three days of TSH-stimulation the I-131 uptake at 24 hours was less than 1%, a pattern consistent with primary hypothyroidism. After adequate treatment with Synthroid, his lipid electrophoresis revealed a return to type IV pattern (January 10, 1972: Cholesterol 297 mg%, triglycerides 302 mg%, serum slightly cloudy, β -lipoprotein normal, pre- β -lipoprotein increased).

Strisower *et al.* (1970) also stated that no untoward lipoprotein shift occurs in type III disorders but they do not mention the possible changes in type V disorders. We have not seen any lipoprotein shift in type III disorders but have seen one in type V pattern:

Mrs G.H. was 62 years old and had diabetes mellitus, treated by Orinase and a history of myocardial infarction in September 1969. Her weight was considered normal at 64 kg (141 lb). On 2/15/70 she had a routine lipid electrophoresis which showed a serum cholesterol concentration of 303 mg% and triglycerides 485 mg%. The patient showed chylomicronaemia and hyper-pre- β -lipoproteinaemia, consistent with phenotype V. At the second lipid evaluation (3/23/70), one month after institution of a low-carbohydrate diet, emphasizing lean meats, fish and the use of polyunsaturated fatty acids, the cholesterol level was still elevated with 279 mg%, triglycerides had decreased to a normal level of 122 mg%. The phenotype V was changed into type II with hyper- β -lipoproteinaemia. Because of the obvious conversion of a type V to a type II disorder, the patient was followed closely without any changes in the dietary regime. This resulted in a decrease of the cholesterol to 256 mg%, further decrease of triglycerides to 98 mg% and eventually a normal lipoprotein pattern.

We would not have known anything about her transient hyper- β -lipoproteinaemia had we not examined the blood at this particular time. The recommendation by Strisower *et al.* of serial paper electrophoretic strips of patients undergoing drug therapy may, therefore, be extended to patients undergoing dietary treatment in order to gain more insight

into the problem of iatrogenic conversions of one hyperlipoproteinaemia type into another.

VI. CHANGES IN β -LIPOPROTEINS IN CASES OF HYPERLIPOPROTEINAEMIA TYPE II DURING WEIGHT REDUCTION

It is generally agreed that most cases of hyperlipoproteinaemia type II are more resistant to dietary changes than any other type of hyperlipoproteinaemia. Again, there are only very few reports in the literature. Wilson *et al.* (1971) stated that adherence to the American Heart Association (AHA) diet by 59 non-obese individuals caused a slight decrease in serum cholesterol concentrations of 9.7% by the end of the first month but only a slight further decline during the remaining five months in this experiment. On the other hand, serum β -lipoprotein levels fell rapidly, reaching a mean of 12.6% below baseline at one month and subsequently declined further to 17.3% below the initial mean level at the end of the sixth month. Among eight individuals with type II disorder the cholesterol level decreased 13.3% whereas the β -lipoprotein level decreased 20.5%. This indicates a greater responsiveness of the β -lipoproteins to dietary changes compared to serum cholesterol concentrations. The following three personal observations are added to clarify some of the problems involved in the dietary treatment of patients with hyperlipoproteinaemia type II.

First Case Report (Fig. 3)

J.B.P., a 53-year-old physician came to our clinic on 3/4/70 grossly obese. His weight was 92 kg (202 lb); his height was 175 cm. The lipoprotein analysis showed β -lipoprotein increased, pre- β -lipoprotein increased, hypercholesterolaemia—336 mg% and hypertriglyceridaemia—335 mg%. The data were consistent with hyperlipoproteinaemia type II. On 6/4/70, three months after the initial diagnosis, the weight had been reduced by 16 kg (36 lb) and the lipoprotein analysis revealed pre- β -lipoprotein still increased. β -Lipoproteins were normal, cholesterol—250 mg%, triglycerides—normal with 118 mg%. On 9/11/70, the β -lipoproteins and pre- β -lipoproteins were reported as “normal” although cholesterol was again increased to 310 mg%, triglycerides stayed normal with 120 mg%. At this third examination, the weight had been reduced to 68 kg and a seasonal effect on the cholesterol level must be taken into account with a lower level in June and an increase again during the fall.

After normalization of his weight to 67 kg (147 lb) the patient was re-examined on 11/24/70. The β -lipoprotein and pre- β -lipoprotein again were reported “normal”; the cholesterol remained elevated at 330 mg% whereas

the triglycerides had further decreased to 85 mg%. The last lipid analysis was done in March, 1972. With weight maintenance at 67 kg (147 lb) the β -lipoproteins and pre- β -lipoproteins were again reported "normal"; serum cholesterol still elevated with 280 mg% and triglycerides normal with 83 mg%.

The clinical significance of the apparent reversal from hyper- β -lipoproteinaemia to a "normal" lipoprotein pattern, as judged by electrophoresis, reported from two different laboratories, remains

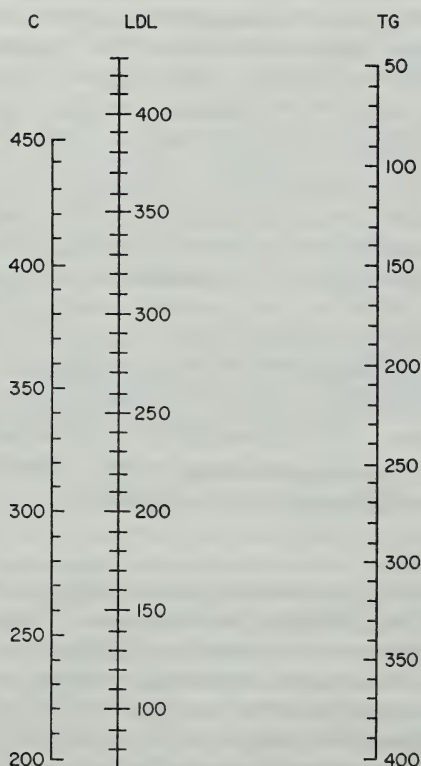


Fig. 2. Nomogram for estimation of plasma LDL concentration (in terms of mg/100 ml of cholesterol in this lipoprotein). This was derived from the equation $LDL = C - (TG/5 + HDL)$ where HDL is assumed to be 45. (Fredrickson and Levy, 1972; Fredrickson, 1972.)

dubious in view of the abnormal low density lipoprotein according to the nomogram recommended by Dr Fredrickson (see Fig. 2). From the dietary standpoint, no further decrease of the cholesterol serum concentration can be expected while continuation of the low-carbohydrate and restricted-fat diet will guarantee the maintenance of a normal triglyceride level in the serum. The cholesterol in the food is limited to

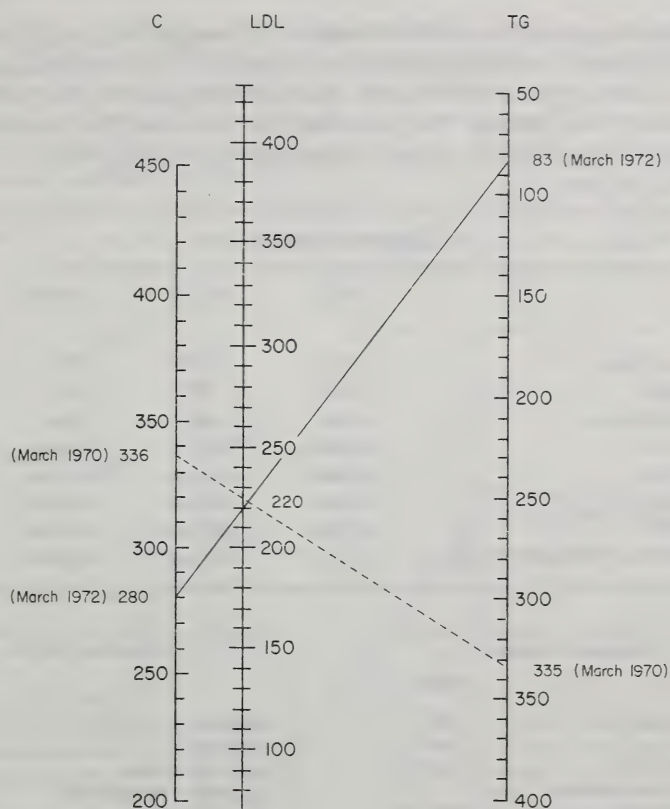


Fig. 3. First case report: Dr J.B.P. aged 53. Low density or β -lipoproteins are practically unchanged between March, 1970 and March, 1972. The desirable levels are 220 mg% or less for cholesterol and 140 mg% or less for triglycerides, connected with an LDL of 140–170. During weight reduction, the excess VLDL was metabolized to LDL which disappears more slowly. Technically, this represents a conversion from type IIb to type IIa.

less than 300 mg, the calories derived from fat amounts to 35% of the caloric intake and a major portion of it consists of polyunsaturated fatty acids.

Second Case Report (Fig. 6)

Mr A.L., aged 57 years (height 182 cm, weight 127 kg: 280 lb) came on 1/6/72 for the treatment of severe essential hypertension (on several occasions 190/110 and 180/130 for the past 10 years). At the age of 17 years his weight had been normal at 74 kg (162 lb).

Within two months, his blood pressure dropped under weight reduction to 150/115, 145/100, 140/95, 135/95, 142/92, 138/90, 134/88, 128/86 mmHg after losing 26 kg (58 lb). On 3/6/72 his weight was 109 kg (222 lb), on 5/29/72, 87 kg (192 lb), remaining at this level until 2/5/73.

Lipid electrophoresis prior to the start of the weight reduction programme on 1/6/72 revealed hyperlipoproteinaemia, type II. This normalization was aided by adhering to a 700 calorie diet consisting of 25 g fat, 60 g carbohydrates and 60 g protein. Weight reduction was aided by weekend fasting from Friday night until Monday morning permitting only non-caloric liquids ad libitum.

Lipoprotein analysis

	1/6/72	3/6/72	5/29/72	2/5/73
Cholesterol, total	358	249	253	220
Triglycerides	100	180	112	113
Serum observation	clear	clear	clear	clear
Chylomicrons	absent	absent	absent	absent
β -Lipoprotein	increased	normal	normal	normal
Pre- β -lipoprotein	normal	normal	normal	normal
α -Lipoprotein	normal	normal	normal	normal
Data consistent with phenotype	II	normal	normal	normal

Lipoprotein analysis		Results
Cholesterol, total	_____	358
Triglycerides	_____	100
Serum observation	_____	CLEAR
Lipoprotein electrophoresis		
CHYLOMICRONS	_____	ABSENT
BETA LIPOPROTEIN	_____	INCREASED
PRE-BETA LIPOPROTEIN	_____	NORMAL
ALPHA LIPOPROTEIN	_____	NORMAL
Data consistent with phenotype	_____	II
according to Fredrickson		

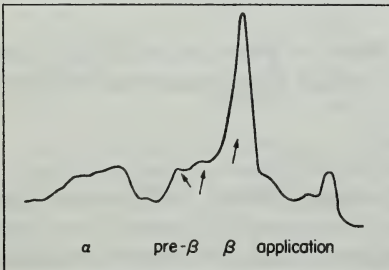


Fig. 4.

Lipoprotein analysis		Results
Cholesterol, total	_____	249
Triglycerides	_____	180
Serum observation	_____	CLEAR
Lipoprotein electrophoresis		
CHYLOMICRONS	_____	ABSENT
BETA LIPOPROTEIN	_____	NORMAL
PRE-BETA LIPOPROTEIN	_____	NORMAL
ALPHA LIPOPROTEIN	_____	NORMAL
Data consistent with phenotype	_____	NORMAL
according to Fredrickson		

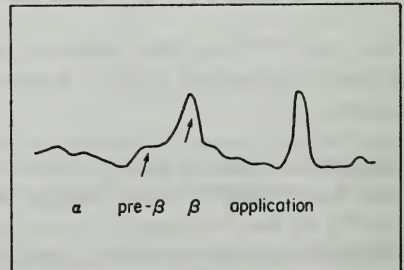


Fig. 5.

The patient frequently ate fish and chicken in larger quantities and therefore on several days each week would eat only approximately half the amount of fat permitted (15 g) and instead increase his protein intake from 60–100 g.

His total intake, however, would never exceed 735 calories per day (100 g protein = 400 calories). The remarkable reversal from a highly abnormal lipoprotein pattern to a normal lipid electrophoresis (see Figs 4 and 5) within the short period of two months is most unusual. The nomogram according to Fredrickson showed a normal low density protein after the weight became normal (see Fig. 6).

Weight maintenance and strict adherence to a 1600 kCal diet, with polyunsaturated fatty acids amounting to $>10\%$ of his total caloric intake, resulted in a further drop of the cholesterol concentration to a normal level (Feb. 1973).

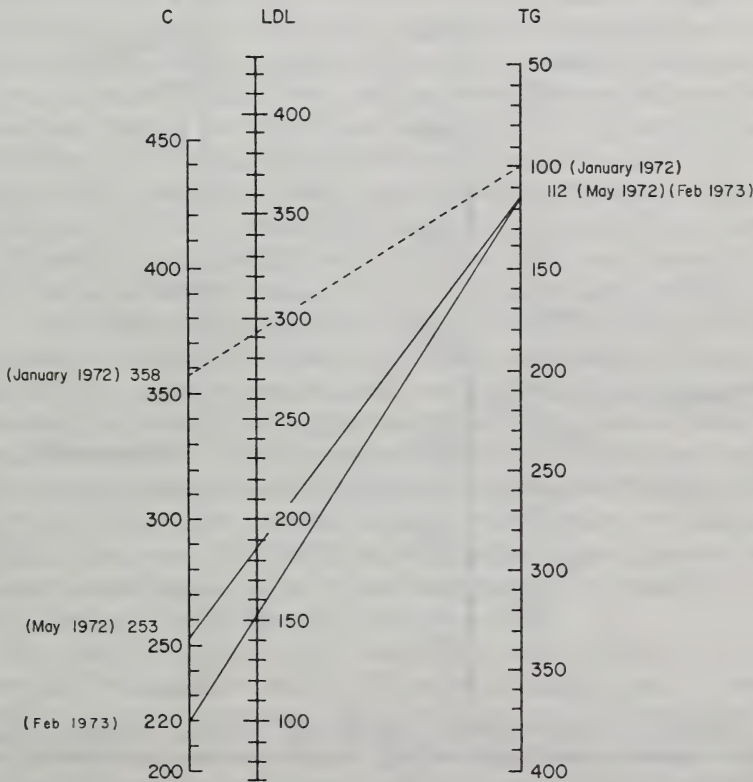


Fig. 6. Second case report: Mr A.L. aged 57. After 40 kg (90 lb) weight loss, LDL decreased from 292 to 185 within five months, after one year LDL was normal.

Third Case Report (Fig. 7)

Mrs M.G., aged 44 years, had known about her hypercholesterolaemia for many years and had been treated with thyroid medication for 24 years and, in addition, with nicotinic acid for one year. Since she had developed rhythm abnormalities shown by ECGs we discontinued the thyroid medication. The nicotinic acid was stopped because it had no apparent effect on her cholesterol

level. Since the age of 20 she had gained approximately 31 kg (68 lb) and her present weight of 84 kg (184 lb) was regarded as at least 21 kg (46 lb) overweight (12/2/70).

The lipoprotein analysis revealed cholesterol—315 mg%, triglycerides—280 mg%, β -lipoproteins increased and the pre- β -lipoproteins increased, consistent with phenotype II. Within five months, the weight was lowered to 64 kg (141 lb) and the triglycerides decreased to 80 mg%. The cholesterol level

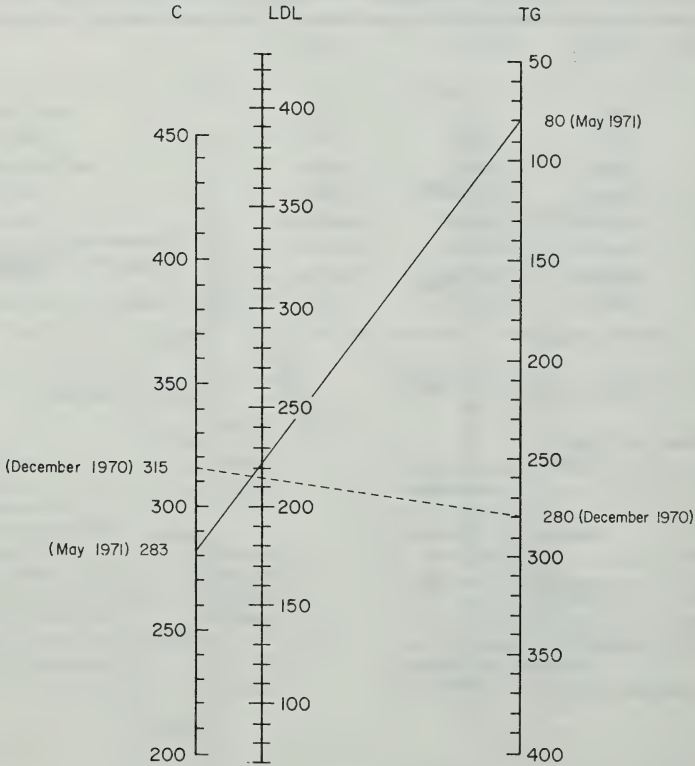


Fig. 7. Third case report: Mrs M.G. aged 44. LDL remained practically unchanged although cholesterol decreased slightly and triglycerides became normalized after 19 kg (42 lb) weight loss.

had only slightly decreased to 283 mg% (5/1/71). However, the possibly misleading electrophoretic finding, which was again confirmed at a later lipid electrophoresis on 7/26/71, was that β -lipoproteins were "normal", pre- β -lipoproteins were normal and the data were consistent on both occasions with a "normal phenotype". With the weight reduction of 19 kg (42 lb) and adherence to a diet low in fat and extremely low in cholesterol (less than 200 mg), the abnormal phenotype II supposedly had changed into a "normal pattern". The decrease in the serum cholesterol concentration between December 1970

and summer of 1971 could be solely explained by the seasonal changes. One must keep in mind, however, the presently used method of analysing lipid patterns. According to the nomogram by Dr Fredrickson the patient has not changed the β -lipoprotein level at all (see Fig. 7).

VII. PRIMARY PREVENTION OF ISCHEMIC HEART DISEASE

1. The primary prevention of ischemic heart disease with dietary intervention has been investigated by a Finnish medical team (Turpeinen *et al.*, 1971). Three hundred and thirteen mental patients without overt ischemic heart disease, in one mental institution, were treated with a diet low in cholesterol, high in polyunsaturated fatty acid, whereas mental patients in another hospital were used as control persons without dietary intervention. Among the 313 dieters without ECG evidence of ischemic heart disease, 17 developed such evidence* (annual incidence rate per 1000 was 14.4). Among 241 control persons without evidence of ischemic heart disease by ECG, a total of 30 developed ischemic heart disease* (annual incidence rate per 1000 was 33.0). The difference in new development of ischemic heart disease in the two groups was significant with $P < .01$. The first study lasted from 1958 to 1965. In March 1965, the study protocol called for a switch-over in the experiment, changing the control hospital into the experimental hospital with dietary intervention and leaving the mental patients in the former experimental hospital as controls. Cholesterol levels decreased immediately in the new experimental hospital and increased in the control hospital with a difference of 30 mg %. By 1971, more cases of ischemic heart disease were diagnosed by ECG in the control hospital than in the experimental hospital but at that point in time, the number of new cases was still too small to reach a statistically significant difference (see also p. 322).

2. The Anti-Coronary Club in New York was initiated in 1957, inventing the Prudent Diet with a P/S ratio 1.25–1.50 (usual American Diet P/S ratio 0.3/0.4), 400 mg dietary cholesterol, total fat intake 33 % and 1.6 g dietary sodium. Archer (reported by Stamler, 1971) recorded in 1969 the incidence of new coronary events: during the 3954 person-years of active experience, accumulated by the 941 experimental subjects, 37 new coronary events occurred. This represents an overall incidence rate of 6.8 per 1000 person-years of experience. The 457 men of the control group, in comparable age categories, have accumulated 3122 person-years of experience and 51 new coronary events, resulting in an age-adjusted incidence of 13.4 per 1000 person-years of experience.

* This includes deaths from coronary heart disease (CHD).

Interestingly, an inactive experimental group (532 men) evolved, shifting from active to inactive status. The observed incidence rate was 7.8 per 1000 person-years of experience, representing 42 new coronary events, predictably a rate between the active experimental and the control group. Total observation time was 12 years.

As expected by the lower total fat intake and the rather drastic restriction of dietary sodium, the number of obese subjects and hypertensive subjects in the experimental group declined at the same time when the main thrust was lowering of cholesterol levels (Rinzler, 1968). After four years of observation, the percentage of obese persons in the experimental group declined from 56% to 18%, the percentage of hypertensives from 26% to 10%. In contrast, the control group had 45% obese at entry and after four years still 44%. Among the control persons, 11% were hypertensive at entry into the study and after four years 13% were hypertensive. Hypercholesterolaemia (260 mg% or more) was found among 43% of the experimental group at entry and declined to 20% after four years. In the control group, 38% were defined as hypercholesterolaemics and after four years, 32% still belonged to this group. After initial weight reduction, the maintenance diet contained 23% protein, 47% carbohydrates, 30% fat, less than 300 mg cholesterol.

3. The only dietary study under double blind conditions was conducted in an elderly male population, living at a Veterans' Administration Centre in Los Angeles (Pearce and Dayton, 1971). In an eight-year controlled clinical trial of a diet high in polyunsaturated vegetable oils and low in saturated fat and cholesterol, 846 men were assigned randomly to a conventional diet (422) or to one similar in all respects, except for a substitution of vegetable oils for saturated fat (424). Fatal atherosclerotic events were more common in the control group (70 versus 48; $P < 0.05$). It is noteworthy that in Leren's dietary trial and in the second report from the British Medical Research Council (1968) no difference was found in the rates of sudden death between experimental dietary and control groups, whereas sudden death in this Veterans' Administration Study was observed in 27 controls and in 18 men of the dietary group. Also, cerebral infarction occurred more often in controls: 22 versus 13. However, total mortality was similar in the two groups: 178 controls versus 174 "dieters" demonstrating an excess of non-atherosclerotic deaths in the experimental group.

The conclusions of these authors concerning the potential co-carcinogenic influence of this type of dietary changes will be discussed in a later section.

4. A preliminary analysis of the results after seven years of dietary intervention in the Chicago Coronary Prevention Evaluation Program

(C.P.E.P.) in 519 men aged 40–59 years with several risk factors but free of ischemic heart disease, was presented by Stamler (1971). It is important to note that other risk factors such as hypertension, obesity, cigarette smoking and physical inactivity, besides hypercholesterolaemia, were influenced at the same time—a multiple risk factor intervention. Among 377 men at high risk who adhered to a low-fat, low-cholesterol diet, a seven year cumulative age corrected coronary mortality rate of 5 per 1000 was found (2 CHD deaths occurred among 377 adherers). The same analysis revealed an age adjusted coronary mortality rate of 27 per 1000 among the 142 drop-outs (4 actual cases within the same observation period).

The *coronary mortality* rates of adherers and drop-outs were compared with 2916 men from the “Pooling Project”, matched for age, medical and risk factor criteria. The Pooling Project combines the experience of six prospective long-term epidemiological studies of 6640 middle-aged (30–59 years old) men over a ten-year period, i.e. followed without intervention. The coronary mortality rate was 20/1000 (59 actual cases), i.e. similar as the rate of the drop-outs. The rates for sudden death were 2/1000 among C.P.E.P. adherers, 10/1000 among drop-outs and 15/1000 among matched men from the Pooling Project. Death rates combined from all causes were recorded: 27/1000, 36/1000 and 50/1000, respectively.

The author concluded:

“For 377 continuing active participants in the C.P.E.P. . . . total mortality at seven years is 46% lower compared with the experience of 2916 Pooling Project men; CHD mortality and sudden death mortality are 75% and 86% lower, respectively.”

These primary prevention studies—the New York Anti-Coronary Club, the Finnish Mental Hospital Study and the Chicago Coronary Prevention Evaluation Program, with the exception of the Los Angeles Veterans’ Administration Domiciliary Center Study—have not been designed as double blind group studies and are, therefore open to criticism. But the combined findings indicate that change in living habits, particularly diet, is associated with decreased incidence or mortality, or both, from ischemic heart disease.

VIII. SECONDARY PREVENTION OF ISCHEMIC HEART DISEASE

1. The first dietary intervention study for patients with myocardial infarction (MI) was conducted by Lyon *et al.* (1956). One hundred and fifty-five patients adhered to a low-fat, low-cholesterol regimen

(a maximum of 50 g fat, 200 mg cholesterol per day) whereas 125 patients without dietary intervention were followed. Both groups had comparable β -lipoprotein levels at the onset of the study. Diet intervention caused a significant decrease in these β -lipoprotein levels, whereas no change occurred in the control group.

The treatment lasted three years and eight months in the experimental group, with 15 re-infarctions, in contrast to 51 re-infarctions in the control group followed for four years and two months. After an average follow-up period of about four years the treated group had a statistically significant lower fatality rate: 2.6 versus 10.0% mortality rate due to recurrent myocardial infarction.

Several authors have criticized that the investigators failed to give any information concerning the criteria of admission to the study, the criteria for the diagnosis of re-infarction and for the methods of judging adherence to the diet (Oliver, 1966; Stamler, 1967). While it is true that in the 1970s a study without this additional information would not be acceptable to medical journals it should be remembered that, back in 1956, somebody had to first conceive the idea of dietary therapy. It is felt that this pioneer work definitely has its place in the history of dietary intervention trials.

2. Another secondary prevention trial was reported during the same year (1956, and last report 1965) by Nelson, with a follow-up of 88 diet-adhering and 154 non-dieting patients with myocardial infarction (a total of 100 patients with previous MI were forced to eat in restaurants and were, therefore, unable to follow the dietary instructions and 54 patients did not adhere to the diet). These two groups, 100 and 54 patients (mean age 58) were used as controls to the 88 patients (mean age 56) adhering and responding to the diet—50–60 g fat/day with emphasis on polyunsaturated fatty acid intake with cholesterol levels decreasing (in two-thirds of diet-adherers, the serum cholesterol concentration was lowered more than 10%). No objection can be raised to the use of non-adherers as controls, since the two groups were comparable in age, sex, heart size, ECG abnormalities and patients with normalized ECG.

In the experimental treatment group, only 31 CHD deaths occurred during 10–13 years of observation (mortality of 35%). In contrast, the mortality from atherosclerotic heart disease in the control group was much higher: 122 (=79%). Thus at the end of the 10–13 years of observation period, 57 of the 88 diet-adherers and 32 of the 154 non-adherers were still alive.

3. Morrison (1960) used the same approach, a low-Wat, low-cholesterol diet containing about 1600 calories daily with 20–25 g fat and 50–70 mg cholesterol, 225 g carbohydrates, 120 g protein for 50 patients with

myocardial infarction. It is necessary to remind oneself that the increased use of polyunsaturated fatty acid in dietary therapy was introduced only in the late 1950s and had not been common knowledge among all investigators at that time. However, this approach of a low-fat, low-cholesterol diet, again, led to a sizeable decrease in serum cholesterol concentrations from a mean of 312 mg % to 220 mg %.

Likewise, total lipids and neutral fats declined markedly. Unfortunately, a few uncooperative patients were dropped from the original treatment group and new cases were added, possibly introducing a degree of bias.

The mortality experience was quite different from that of a control group of 50 patients who were left with their own dietary habits. After eight years, survival rates were 56 % for the treatment group and 24 % for the control group. After 12 years, the mortality was 62 % in the dietary group and 100 % in the control group. Oliver (1966) objected to the study design and execution since there was a marked weight reduction in the treatment group and no weight loss in the control series. Furthermore, he criticized that the study was not conducted in a double blind fashion and the degree of surveillance of the treatment group was greater than that for the control group. We feel that it was just this particular aspect, the intensive guidance through a dietary programme for the 50 patients in the experimental group which led to the success not only in the most important aim, the reduction in mortality compared to a control group, but also in the other objective measurements—weight loss and decrease in cholesterol levels. If the control group had been followed similarly with some dietary control, they too would have lost weight and they might also have decreased cholesterol levels and would not have constituted a control group as such. Studies conducted under double blind procedures are extremely expensive and are hard to manage in the free-living population. Even in an institutionalized population group as observed by Dayton and co-workers (1969b), a sizeable proportion of the experimental group did not adhere to the dietary intervention.

4. For three years, Koranyi (1963) followed survivors of myocardial infarction who were treated with a low-fat diet (35–40 g per day) and control patients without dietary restrictions. The serum lipids were not measured but the mortality after three years of observation showed marked differences: 8.6 % in the dietary group and 19.7 % in the control group.

5. Hood *et al.* (1965) from Sweden reported a retrospective study over a 17-year observation period. A group of 112 patients with previous myocardial infarction or angina pectoris or with essential hypercholesterolaemia was compared with a control group. The 112 control

patients were matched by sex, age, blood pressure, degree of vascular symptoms and cholesterol levels. In the control group there had been either none, minor, or inconsistent dietary alterations. Both groups consisted of 61 women and 51 men.

The management of the treated group incorporated a low-fat, low-cholesterol diet with the addition of 50–60 g of oils high in polyunsaturated fatty acids. Mean serum cholesterol concentrations were reduced by 20% in the diet group and 6% in the control group in women. Among the dieters, four women died and among the control group 18 women died during the observation period. The favourable mortality experience in females was also observed in males. There were 21 males in the diet group who previously had a myocardial infarction and two of them died. Of the 21 males with myocardial infarction in the control group, 12 died. However, the mean serum cholesterol concentration decrement in the diet group was only 7%, whereas in the control group it was 14%. There is no apparent explanation for the discrepancy in the findings among male and female patients as far as cholesterol levels are concerned.

6. A study by Leren (1970) in Norway dealt with 412 men, aged 30–64 years, randomized into two groups one to two years after their first myocardial infarction. For the experimental group a diet low in saturated fats and cholesterol (264 mg/day) and high in polyunsaturated fats (soyabean oil) was recommended. Fat comprised 39% of the total calories and contained 55 g (52.7%) polyunsaturated fatty acid and 22 g (21.6%) saturated fatty acid with a P/S value of 2.4. After five years the incidence of fatal and non-fatal myocardial reinfarction was found to be significantly reduced. Sudden death was uninfluenced. Major coronary heart disease relapses, including fatal and non-fatal events (myocardial infarction), were significantly less ($P = 0.05$) among the 206 men placed under dietary management compared to the control group.

After 11 years, death from all causes had occurred in 101 of the original dieters and 108 controls. A significantly reduced myocardial infarction mortality in the original diet group was found (32 versus 57, $P = 0.004$). The total number of coronary deaths (fatal myocardial infarction and sudden death) was 79 in the diet group and 94 in the control group ($P = 0.097$).

The CHD mortality was correlated with age, serum cholesterol level, blood pressure, body weight, smoking habits, and a combination of these risk factors. When combining data from both groups, a three-fold greater CHD mortality rate was demonstrable among the hypercholesterolaemic, hypertensive smokers than among those in whom these factors were low or absent.

7. Bierenbaum *et al.* (1973) presented data of a 10-year observation

period with dietary therapy. One hundred men, 30–50 years old, with documented coronary artery disease and past myocardial infarction, were placed under dietary management with a 28% of cal. fat diet. One hundred men whose diets were not managed were matched with regard to age at entry to the study, age at infarction, number of infarctions, blood pressure level, degree of angina, and serum cholesterol level among other factors. Over a period of five years the diet-managed group experienced and maintained a significant reduction in serum cholesterol level which the non-diet-managed group did not.

“Over a period of 10 years there were significant reductions in serum-lipids in the diet-managed group compared with the control group. In this predominantly lipoprotein-phenotype IV group, using a diet containing less than 9% of calories as saturated fats and less than 400 mg exogenous cholesterol daily, the degree of unsaturation of the diet did not appear to influence either serum-lipid values or mortality rates. After 10 years, the diet-managed group had a 17% greater survival-rate than the control group (in comparison to the control group $P < 0.05$!). This is especially true of the younger men, who were under 45 years when they entered the study. In this under 45-group, incidence was over twice as high in the control group as in the study group. Even in the over-45 group, the incidence in the control group was one-third higher than in the study group . . . Dietary change instituted after 45 may still be beneficial.”

The authors repeatedly mention the importance of weight reduction in the study group. After weight normalization, the study group was on approximately 2000 calories, 20.4% derived from protein (102 g), 27.8% derived from fat (61.8 g) and 51.8% from carbohydrates. It seems particularly remarkable that all individuals in this study were followed up for 10 years. No subject was lost to the study for any reason except death. To enable the men to adhere more easily to the prescribed diet for protracted periods, specially prepared frozen dinners, including pies, and ice-cream substitute, and oil, were obtained from a project store at reduced prices.

The following four studies constitute the only dietary intervention trials in the world literature which did not demonstrate the influence of dietary intervention: they were all conducted in England. The first was a four-year study of patients with myocardial infarction; after three years of treatment with corn oil (60 g daily) the “cholesterol level decreasing effect became weaker”. The mortality rate among 28 patients within two years was 14.3% which was reportedly slightly higher than in a control group of male patients also with myocardial infarctions under anticoagulant therapy (Watson, 1963).

The second study (with dietary intervention) (Rose *et al.*, 1965) lasted only two years and was conducted in three small groups (28, 26 and 26 patients). An 80 g "oil cocktail" was given daily which, in many patients, led to the discontinuation of oil intake because of development of diarrhoea, nausea and distaste. The experimental group was placed on corn oil, the control group on olive oil and the second control group was left without advice on dietary fats.

Of the 28 patients in the corn oil supplemented diet group, 52% remained free of re-infarctions after two years. Of the 26 patients in the olive oil supplemented control group, 57% remained free of reinfarction and of the 26 patients in the second control group without dietary intervention, 75% remained free of re-infarctions. The interpretation by the investigators was that under the

"circumstances of this trial, corn oil cannot be recommended as a treatment of ischemic heart disease; it is most unlikely to be beneficial, and it is possibly harmful."

This conclusion is not warranted from a short-term investigation with such small numbers of patients involved. There is no question that the statistical design of the study was sound. However, the only conclusion permissible is that it was a valuable pilot study for a future project, employing a different method of application of the use of oils in cooking and baking, as well as enlarging the number of subjects to be studied.

During the same year (1965) the British Medical Research Council published the results of a study of 252 patients with myocardial infarction (123 in the dietary group and 129 control patients without dietary therapy). The follow-up extended from 1957 through 1963. Already after one year, the cholesterol levels in the experimental group and the control group were no longer significantly different. The patients in the control group, without dietary advice, may have been influenced by the general trend in public education programmes and decreased their fat consumption. The method of this experimental design must have encouraged the control patients to pay more attention to their dietary habits since all patients, including the controls, had to record the foods eaten during the first seven weeks on a certain day each week and later always on the first day of each month, including weighing foods to be consumed. In addition, regular interviews of dietary habits were conducted and the weight was measured.

After five years, the final results were not different in the two groups: the experimental group experienced (among 123 patients) 46 re-infarctions and 10 deaths from myocardial infarction. Among the control

group (129 patients), 48 experienced re-infarctions and 12 died of myocardial infarction.

The fourth study in male patients under the age of 60, again conducted by the British Medical Research Council (1968) also used "oil cocktails" (43 g daily plus 42 g of soyabean oil for cooking). Among the 199 patients in the dietary experimental group cholesterol levels decreased from a mean of 272 mg % to 213 mg %. Sixty-two men had a re-infarction (31 %). The 194 patients in the control group, without dietary advice, showed cholesterol level decreases from a mean of 273 mg % to 259 mg %, 74 patients had re-infarctions (38 %).

The authors expressed surprise that their results did not show the same beneficial effect of a diet low in cholesterol, high in polyunsaturated fatty acid in the treatment of patients with myocardial infarction as had been reported by Dr Leren from Oslo. The main difference in the selection of patients was that the Norwegian patients had stabilized their myocardial infarction according to the study protocol at least 20 months prior to entry into the study. In contrast, the British study admitted patients after an average of 36 days following the acute event. It is well known that the re-infarction rate is highest during the first year and diminishes progressively during subsequent years. Another difference between the two studies is that less than 50 % of the patients in London continued the experiment for four years whereas all patients in Oslo adhered to the regime for five years, except, of course, those who died. Therefore, a great number of patients in London were unable to possibly benefit from the long-term use of polyunsaturated fatty acids as was the case in the Oslo study. This last report by the British Research Committee (1968) concluded:

"There is no indication that this type of diet affects mortality. The combined evidence, however, suggests that a proportion of non-fatal re-infarctions might be prevented, though more evidence is required to confirm this effect."

In view of the cancer mortality reported from the study by Pearce and Dayton (1971) it is interesting to note that in the experimental dietary group after seven years of observation one cancer occurred (= 0.5 %) whereas six cases of fatal carcinoma were observed in the control group (3 %)—another proof that the long-term use of polyunsaturated fatty acid diets is most unlikely to cause or favour carcinogenesis.

IX. THE PRESENT SITUATION IN THE COMMUNITY OF EVANS COUNTY (U.S.A.)

After countless clinical studies and investigations under metabolic ward conditions showing unequivocally positive results of a diet low in

cholesterol, high in polyunsaturated fatty acid in lowering cholesterol levels, the major concern at this time is how to bring about the decrease of serum cholesterol levels in the community. We have investigated this problem during seven to nine years of observation in the Evans County Study in Georgia. Many epidemiologic studies have been concerned with the relationship of hypercholesterolaemia to the development of ischemic heart disease based on the level of hypercholesterolaemia at the intake examination. Relatively little attention has been directed towards epidemiologic study of those individuals in the community who had elevated baseline serum cholesterol concentrations and who subsequently have decreased to normal values.

The purpose of our study in Evans County was two-fold. The first was to define the percentage of people in the total population examined twice (1960-62 and 1967-69) who significantly decreased their cholesterol level. The second goal was to investigate the possible relationship between decreases of cholesterol level and changes in dietary habits in persons remaining free of vascular disease.

Cholesterol levels were determined during *both* examinations in a total of 2272 persons. Of these 1507 were white, 711 white males and 796 white females. The black sample consisted of a total of 765 persons: 321 black males and 444 black females. This sample white to black ratio represents the racial distribution of the total community very closely.

Hypercholesterolaemia was arbitrarily defined as a level of 240 mg/100 ml or above. Changes in cholesterol levels were compared from the intake examinations (1960-62) to the second round of examinations (1967-69). Significant decreases were defined as those occurring in persons who had a baseline serum cholesterol concentration of 240 mg/100 ml or higher which in 1967 had decreased at least 40 mg/100 ml. Persons with decreases of serum cholesterol concentrations were matched for race, sex and age (± 3 years) with control individuals who either remained at their baseline level or had increased levels.

We interviewed each healthy person with significant decreases who remained free of heart disease or strokes, and one control person in order to evaluate reasons for decreases. There were only two refusals. A small number of people had migrated but were known to be alive and healthy. Interviews were conducted in the homes. The questionnaire comprised 26 items, covering major changes in the person's diet between the first and second examination (1960-62 and 1967-69). Medication as a factor in lowering cholesterol levels could be dismissed. We were interested mainly in dietary habits and particularly in changes in the consumption of visible fat and types of meat.

As will be seen, only a few subjects actually decreased cholesterol levels to a significant degree and remained free of vascular diseases.

A. Results

Hypercholesterolaemia (≥ 240 mg/100 ml) at the baseline examination was found almost twice as frequently in females as in males of both races, i.e. 19% in white males but 31% in white females and 13% in black males but 23% in black females (Table 2).

Table 2

Distribution of cholesterol ≥ 240 mg/100 ml by age in race-sex groups, 1960-62

Age (yr)	White males		White females		Black males		Black females	
	Par	Cases	Par	Cases	Par	Cases	Par	Cases
15-24	118	2	108	2	81	0	91	3
25-34	109	15	110	11	43	3	54	2
35-44	167	35	189	43	79	11	111	18
45-54	259	61	239	79	171	33	167	45
55-64	175	42	182	93	89	13	129	44
65-74	110	25	131	71	68	10	90	32
75+	9	3	13	6	6	2	4	2
TOTAL	947	183	972	305	537	72	646	146

Per cent with cholesterol ≥ 240 mg/100 ml

15-24	1.7	1.9	0	3.3
25-34	13.8	10.0	7.0	3.7
35-44	21.0	22.8	13.9	16.2
45-54	23.6	33.1	19.3	26.9
55-64	24.0	51.1	14.6	34.1
65-74	22.7	54.2	14.7	35.6
75+	33.3	46.2	33.3	50.0
TOTAL	19.3	31.4	13.4	22.6

For white males there is a steady increase in percentage of hypercholesterolaemic individuals up to the age of 55-64 years followed by a slight decrease in the age group 65-74. For white females there is a sharp increase in the prevalence of hypercholesterolaemia at age of menopause (at the ages of 45-54 years, the prevalence is higher than in males of the same age) and a further increase of hypercholesterolaemic subjects after menopause (twice as many females as males of the same age group). For black males except at the age of 45-54 years, there is no sizeable

increase in percentage of hypercholesterolaemic subjects at each age. There is a higher prevalence of hypercholesterolaemia in the white than the black with increasing age. The age relationship for black females is similar to that among white persons.

In view of the known relationship of incidence of ischemic heart disease and hypercholesterolaemia in general, the lowering of cholesterol levels was, of course, considered of potential benefit. Fifty-seven white males and females with hypercholesterolaemia in 1960 died prior to re-examination. Of 458 white male and female survivors with hypercholesterolaemia (as defined at the baseline examination) and re-examination in 1967-69, only 34 showed a decrease of cholesterol levels ≥ 40 mg/100 ml and were found free of vascular disease. An additional 23 persons (5%) also had a decrease of cholesterol levels but were diagnosed with vascular disease. It is interesting to note, therefore, that of the total white population with hypercholesterolaemia only 7.4% had significant reductions in serum cholesterol concentrations and were healthy after an average 87-month period.

Among the black males and females, 24 individuals with hypercholesterolaemia died prior to re-examination. Of the 196 survivors with hypercholesterolaemia, only nine persons (5.6%) had a decrease in cholesterol levels ≥ 40 mg/100 ml during the same observation time. In 1967 through 1969 an additional nine black persons (5.6%) also had a decrease of cholesterol levels but were diagnosed as having vascular disease. Table 3 shows the status of the subjects in August of 1970 when an attempt was made to locate all persons with decreases of serum cholesterol level for interviews.

In the hope of eliciting reasons for lowering of cholesterol levels in the general community (where no drug intervention or any other effort had

Table 3

All persons with hypercholesterolaemia (≥ 240 mg/100 ml) at intake examination who survived to the second examination and whose cholesterol values decreased ≥ 40 mg/100 ml

Status, August 1970	57 Whites	18 Blacks
Vascular disease	23	9
Migration, alive and well	6	1
Interviewed, alive and well	27	7
Not interviewed, alive and well	1	1

been directed toward hypercholesterolaemia) we examined the dietary habits among this group (Table 4).

To make the dietary interview meaningful, control persons with high cholesterol levels who either had remained hypercholesterolaemic or

Table 4

Dietary changes—comparison of subjects with decreased cholesterol levels and controls with increased serum cholesterol concentrations^a

Hypercholesterolaemia	27 White males and females	27 Controls
Dietary changes	25 (93%)	17 (63%) ^b
Average no. of changes	3	2
Diabetes mellitus with dietary changes	4	5
Diabetes mellitus without dietary changes	0	1
Medication (thyroid hormones)	4	1
Gastrectomy	1	0

^a White subjects only.

^b Probability significant at the 5% level.

increased further were asked the same questions. Quite marked differences in changes of dietary habits appeared between the "decreasers" (93%) and controls (63%) among whites, whereas numbers among blacks were too small to permit any conclusion. Specific dietary changes are enumerated in Table 5.

The table indicates that more than twice as many persons with decreases of cholesterol levels eliminated certain food items from their diets than persons whose cholesterol levels remained at the same level or increased. These changes are particularly interesting in view of the drastic cholesterol reductions among the 27 white persons interviewed. The mean level in 1960–62 was 293 mg/100 ml and in 1967–69, 220 mg/100 ml; the 27 control individuals started at a mean level of 260 mg/100 ml with a subsequent increase in 1967–69 to 289 mg/100 ml (+29 mg/100 ml).

Table 5
Number of individuals who changed dietary habits

Food items eliminated	"Cholesterol decreaseers"	"Cholesterol increasers"
Fried foods	16/27	4/27
Eggs	11/27	4/27
Hard fat	10/27	5/27
Desserts	10/27	5/27
Pork	12/27	8/27

As expected, dietary changes were encountered mainly in diabetics with hypercholesterolaemia regardless of whether they belonged to the "decreaseers" or to the controls: out of ten diabetics nine reported several alterations in dietary customs.

B. Comment

McDonough *et al.* (1965) reported from the prevalence examination in Evans County that blacks "have significantly more calories in the diet" than whites, but that black males weighed less. "Significant differences were noted in animal fat intake", providing more saturated fatty acids and less linoleic acid in the average diet of blacks. In spite of these differences, the cholesterol levels in 1960-62 were significantly higher in whites. The re-examination in 1967-69 revealed essentially the same differences in dietary intake and again fewer black persons with high cholesterol levels than white persons, though not at a significant level.

The conclusion seems unavoidable that cholesterol levels are less influenced by the life-long fat intake among blacks and that once serum cholesterol concentrations are in the high range they do not carry the same high risk as in whites.

The causes of hypercholesterolaemia are still shrouded with uncertainties as to which are more important in an individual case, genetic or environmental (i.e. dietary) factors. However, the influence of diet on hypercholesterolaemia, e.g. dietary manipulation by reducing cholesterol intake and increasing polyunsaturated fatty acids is well documented and has been discussed previously. One purpose of this study was to find the possible effects of dietary influences on hypercholesterolaemic individuals in the community. The number of individuals free of vascular disease displaying a significant decrease of cholesterol levels was distressingly small, leaving only 27 white and 7 black individuals for analysis. It is felt that this small percentage of the hypercholesterolaemic segment of the total community becoming normocholesterolaemic

(7.4 % whites, 5.6 % blacks) is in itself interesting for the planning of future intervention studies.

As far as one can judge from the small numbers involved, changes in dietary customs among the white hypercholesterolaemic subjects who were interviewed might indeed have contributed to the significant reduction of the serum cholesterol level from an initial mean value of 293 mg/100 ml to a desirable mean value of 220 mg/100 ml. We were able to rule out seasonal variations. In only four cases was the first blood sample taken during the winter and the second during the summer. In all other cases, sampling time was identical as far as season is concerned and, therefore, reductions beyond 40 mg/100 ml as cut-off point in this study could not be explained by either seasonal variations nor by intra-individual changes which in reliable laboratories are reported to amount to between ± 5 and ± 20 mg/100 ml.

Age is another factor influencing cholesterol levels in the community. Generally speaking, after a steep increase of cholesterol levels from the age of 20 to 50 years, the serum cholesterol concentrations level off without further increase. This was shown in the prevalence study by McDonough *et al.* However, a decrease after the age of 50 to account for almost 70 mg/100 ml in the 27 white persons who were interviewed has not been reported in any population study. In addition it should be noted that these men and women were spread over the entire age range of the population.

The results of our study may lead one to ask whether it would be desirable or even necessary to change the dietary habits of the black community. We have documented definite overall changes in nutrition in Evans County with the preferential use of vegetable oil and margarine among the white community, whereas the black community still adheres to the traditional way of eating and heavy use of animal fat, in particular salt-rich bacon drippings and lard.

If neither the incidence of cerebrovascular disease nor the incidence of ischemic heart disease—as demonstrated in other publications from this study—is markedly influenced by the cholesterol concentration in the serum of blacks, one might well concentrate on other dietary aspects in blacks. Undoubtedly, the salt content of the diet among black men and women would be a more important target for intervention as a contributing factor in the control of hypertension. Likewise, among blacks the considerably higher carbohydrate and total caloric intake would require dietary advice among the large numbers of black women with decreased glucose tolerance. On the other hand, among whites the results from this study certainly are suggestive of the value of more wide spread use of dietary treatment of hypercholesterolaemia.

X. THE OBLIGATION FOR THE FUTURE OF THE COMMUNITY

Epidemiologic research must now be converted into applied epidemiology on the community level. It seems significant to us that the American Heart Association and the National Heart and Lung Institute are the agencies who have alerted the medical profession and have given fresh impulses to the necessity for profound dietary changes in the American nutrition. Cardiologists and internists, nurses and physician's associates find themselves more and more in the role of health educators. The motivation of potential patients without causing anxiety, the education towards self-responsibility for one's own health without sounding evangelistic and the power of persuasion without overwhelming the patient with scientific facts, is an art. It is predictable that this art, in the years to come, will be a very important quality of the physician in the field of prevention of chronic diseases. Modern medicine is facing two major obligations with regard to hyperlipidaemia: firstly, the finding of asymptomatic patients in the community similar to the case finding of new diabetics and secondly, the motivation of these "healthy" individuals for long-term therapy.* The bridging of the gap between our capacity to treat hyperlipidaemias effectively and the presently insufficient and ineffective application of this knowledge is the task for the future. The National Heart and Lung Institute has recently issued a number of relevant questions to research institutions throughout the United States which we shall try to answer in the following sections.

A. What Educational Programmes can be Developed for Individuals and Groups of Patients with Different Learning Abilities and Backgrounds

In my experience, the best results—regardless of learning ability and background—can be expected from a combination of individual instruction and group therapy. Individual instruction ideally includes family members. Group therapy alone does not seem to be very effective and group therapy in our use of the word should be limited to a free exchange between different members of the same peer group. Individual instruction must be maintained over a long period of time with regular weekly short meetings of ten minutes duration during which the dietary diary is being reviewed with the patient. In the past, many patients have expressed the desire for continuation of keeping a diary, although we felt they did not need to do so any longer. However, the psychological effect of checking one's own dietary intake must be recognized. Review of the diary does not take more than a few minutes. Patients who are

* See also Appendixes I and II of the introductory chapter (pp. 33 and 36).

unable to write are being taught to fill out a diary by simple drawings, e.g. fruits or in case they have used egg whites, drawing the number of eggs they have consumed. If the main dish is fish, a simple F will suffice, if chicken or pork C or P respectively.

We also gave patients, who were unable to write, a postage scale for weighing meat and fish portions. They were taught to watch for three numbers on the postage scale: 12 oz of Haddock fish equals approximately 6 oz of chicken or 3 oz of sirloin roast in caloric value. They were instructed to write these numbers, 12, 6 or 3, down in their diary and this way learn to judge by eyesight how much fish they could consume in comparison to pork or chicken. In summary, the most important part of the educational programme is an individualized regular teaching programme, whereas the free exchange among members of a peer group is of secondary importance. Each individual must be taught to fill out a dietary diary and to use a dietary scale.

In addition to giving out a one page table showing the cholesterol content of certain food items (see Table 6 for example) the dieters

Table 6

Cholesterol content (mg%) in $3\frac{1}{2}$ oz selected foods (limit of cholesterol intake per day: 300 mg)

Dairy products		Seafood	
Egg yolk ($3\frac{1}{2}$ oz)	1400	Oysters	326
Egg (1 yolk)	300	Caviar	300
Butter	300	Lobster	208
Cream	140	Crab	145
Cheddar cheese	100	Shrimp	125
Ice cream	45	Sardines	70
Whole milk (1 cup)	35	Salmon	60
Cottage cheese	15	Halibut	60
Skim milk (1 cup)	1	Herring	58
Egg white	0	Cod	50
		Trout	50
Meats		Miscellaneous	
Brains	2000	Vegetable oils	0
Liver	250-600	Margarine	0
Kidney	400	Cereals	0
Beef	100	Fruits	0
Pork	100		
Veal	90		
Chicken	75		
Turkey	75		
Lamb	70		

should be instructed, simply, how to limit the total intake of cholesterol to less than 300 mg per day, and to increase the polyunsaturated fatty acid intake to more than 10% of the total caloric intake. A person with normal weight and a daily intake of 2000 calories, should consume at least 22 g polyunsaturated fatty acids in order to achieve the 10% level of intake of polyunsaturated fatty acids. However, in a person who needs to reduce weight, e.g. on a 1000-calorie diet, the same prescription would give the patient 20% of his total intake in the form of polyunsaturated fatty acid.

B. How Can Patients be Stimulated to Follow Diet Modifications for Extended Periods of Time?

Any diet modification de-emphasizing animal fat but emphasizing the use of fresh fruits, salads, vegetables, skim milk products and lean meats and fish will produce a general feeling of well being. This, in our experience, has been the most powerful stimulant to follow the diet modifications for extended periods of time. In other patients it may be the discontinuation of drugs which will encourage the patient more than anything else; in another group of patients it is the close participation of the patient in the follow-up of his own laboratory studies, be it cholesterol, uric acid, glucose, blood pressure levels or, as exemplified in two cases. ECG changes over a relatively short period of time.

The first patient was a 49-year-old white male who was informed about negative T waves in his chest leads (the only abnormal finding in an extensive endocrinologic work-up). His weight was 164 kg (360 lb) when the first ECG was taken. The second cardiogram was taken after a weight loss of 13.6 kg (30 lb) and the third ECG was taken after losing a total of 31.8 kg (70 lb) (Fig. 8). He was referred to us by the Vocation and Rehabilitation Service since he was unable to find a job due to Pickwick Syndrome. His regained mental alertness and the knowledge that abnormalities in his ECG had disappeared during weight reduction made him a most cooperative patient. (See pp. 88-89: note T wave changes from left to right.)

The second ECG was done on a 39-year-old black female whose weight on 10/9/70 was 173 kg (381 lb). On 9/19/70 after her weight had been reduced to 163 kg (358 lb) the ECG showed definite improvements in her T waves and on 11/13/70 when she had reduced her weight to 154 kg (339 lb) the abnormalities from the first ECG had been eliminated (Fig. 9). This patient, who was unable to read or write, was more impressed by the negative and, later, positive T waves than by the fact that she had chemical diabetes mellitus. The diabetes disappeared when she weighed 127 kg (280 lb).

Other patients are more influenced by family history and by observation of the same disorder among friends and relatives. In summary, it

is the time involvement of the physician, his willingness to let the patient—regardless of his background—participate in the laboratory and ECG studies which bring about the best stimulation for patients to follow diet modifications for extended periods of time. It is, in short, the physician's concern and personal interest which leads to the patient's recognition of his own responsibility for his health.

C. What are the Characteristics of Individuals with Good and Poor Adherence? How can this Information Assist in Planning Patient Nutrition Programmes?

Obvious candidates for poor diet adherence are patients with psychiatric histories, alcoholism and nicotine addiction. It is our personal experience that the group with the poorest prognosis for diet adherence is the group of white, female cigarette smokers. The fact that all other race/sex groups are able to quit smoking when requested seems to be a good indicator of future diet adherence. We also agree with the finding by Stamler (personal communication, 1972) that patients weighing over 136 kg (300 lb) are a relatively poor risk for future success in any dietary programme. Another important factor is the cooperation of members of the patient's family. Ideally, all members involved in buying and preparing food should be instructed at the time of the first instruction of the patient. It is often possible from the first interview to assess the willingness of the family to cooperate with dietary changes. It is equally important to realize that in a female patient with lipid abnormalities, the full understanding of the problem is required from her husband. However, if he shows no interest in dietary changes in his household, the entire programme may be jeopardized (Heyden *et al.*, 1973).

At the time of the first interview it is, therefore, valuable to ask a few questions, regarding past history of psychiatric disorders, alcoholism, cigarette smoking habit, weight history and maximum weight in the past, and the expressed assurance of interest of family members in the dietary changes of the patient. The distance from the clinic and mode of transportation to and from the clinic, and the working hours of the patient in relation to clinic hours also need to be taken into consideration.

D. How Can the Programme be Evaluated by the Patient, Nutritionist and Physician?

The most objective evaluation of a successful dietary programme is, of course, the improvement or normalization of the laboratory result. Laboratory results, however, may not always be influenced by the dietary changes suggested and adhered to by the patient. Two other possibilities are the weekly follow-up with a dietary diary composed by

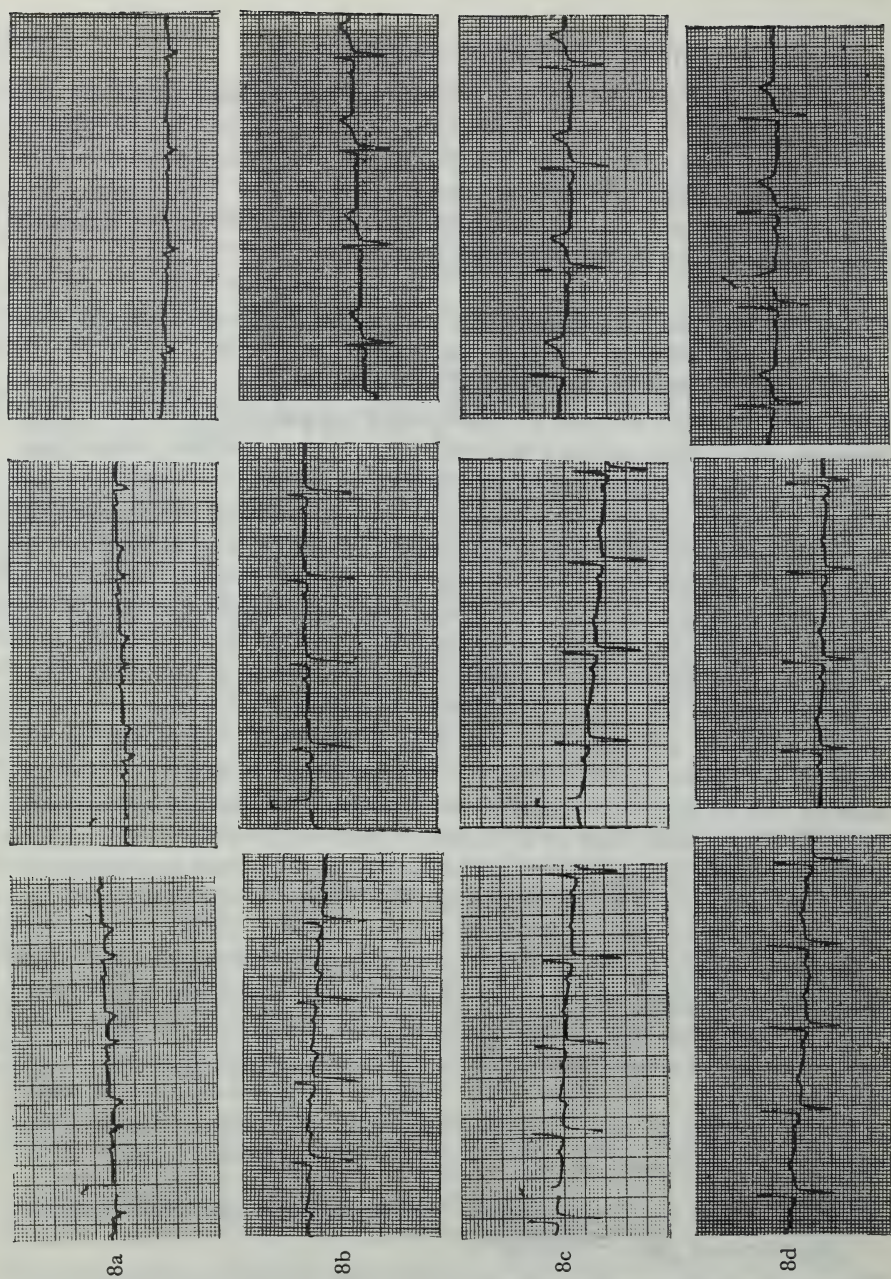


Fig. 8. ECG changes after weight loss from 164 kg (360 lb) to 150 kg (330 lb) to 132 kg (290 lb).

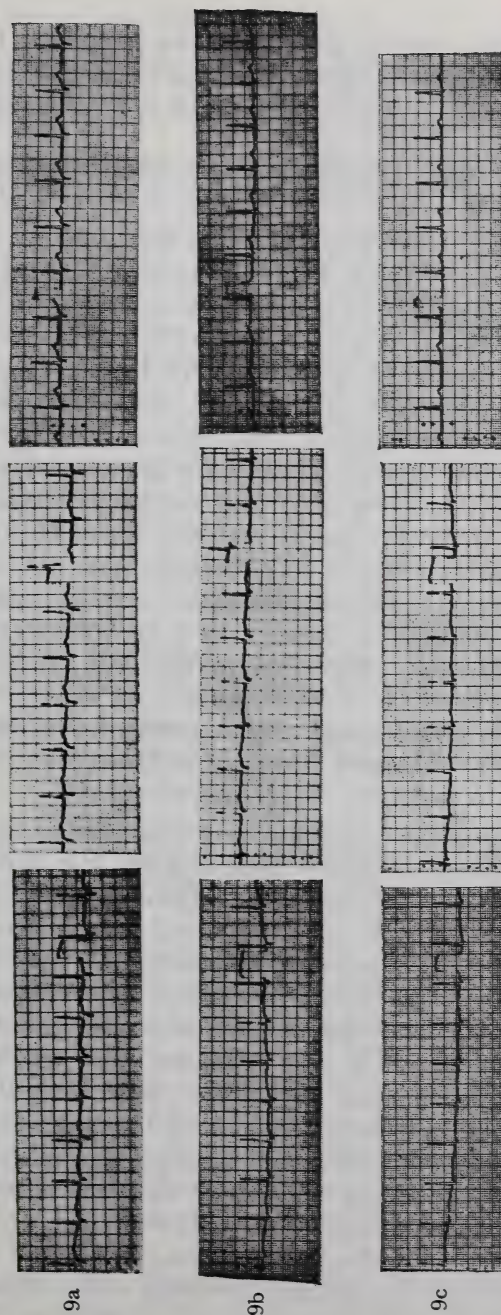


Fig. 9. ECG changes after weight loss from 173 kg (381 lb) to 163 kg (358 lb) to 154 kg (339 lb).

the patient and/or a visit by the nutritionist or nurse to the home of the patient at unannounced times, e.g. dinner or lunch time, checking the ingredients and weighing the food portions to be consumed.

E. How Can the Educational Programme be Taught to Nutritionists?

It has been customary in our institution that a dietetics intern follows the physician in the Cardiac Rehabilitation Clinic held once a week in the afternoon, observing the individual instruction of a patient and his or her spouse. Since dietary habits are uniformly rather poor, common dietetic errors in persons with abnormal lipid values may be brought out in several interviews from past dietary habits. The preoccupation of some nutritionists with various vitamin deficiencies of diets at a time when multi-vitamin capsules are available in a great number of different preparations needs to be replaced by a concern for the hidden sources of cholesterol, of animal fat and of "empty" calories. These individual training sessions with only a few patients probably do more for the education of a nutritionist than classroom lectures. Ideally, they should be followed by placing a single patient into the responsibility of a dietetic's intern under the supervision of the physician.

F. What Knowledge Does the Nutritionist Need in Order to Work Effectively with Physicians Concerning the Patient's Nutritional Needs?

The modern nutritionist must have a definite knowledge of the cholesterol content of beef, chicken, seafood and fish, e.g. in three-ounce units in order to assess quickly the total cholesterol intake of a daily menu and whether more than 300 mg of dietary cholesterol has been consumed in one day. She needs to know the definite advantage of corn, sunflower and safflower oil versus peanut oil and coconut oil and their effect on cholesterol levels rather than the vitamin concentration in certain vegetables and fruits. She must know how to apply polyunsaturated fatty acids in margarine and vegetable oils into calorically restricted and calorically unrestricted diets, e.g. stressing the different caloric values of a tablespoon of vegetable oil versus a tablespoon of margarine. She ought to be prepared to suggest recipes for skim milk "milk shakes", for sherbets with the use of egg whites without cream or whole milk, etc. All this requires a rather limited knowledge which can be taught within a few hours, but the nutritionist also needs to be thoroughly informed about the major diseases which may be effectively prevented by treatment of certain risk factors through nutritional habits and dietary changes (hyperlipoproteinaemia, hypercholesterolaemia, hypertrigly-

ceridaemia, hypertension, hyperglycaemia and hyperuricaemia). This latter part may need considerably more time.

G. What Efforts Can be Made to Increase the Exchange of Information Between Nutritionist and Physician?

Diets must be ordered in a similar fashion as a medical prescription of drugs with an accompanying explanation as to what can be expected from a particular change and possible side effects. The dietitian-nutritionist should be given more detailed information in disease processes. It is insufficient simply to give her an order for a specific diet. An increase of the exchange of information between the nutritionist and physician can only be expected by mutual respect and is best taught on an individual basis following and cooperating with a single patient. The nutritionist has to learn how to search for hidden sources of cholesterol and animal fat in a patient's regular diet which may enable the nutritionist to advise the patient about the necessary changes. Questions regarding the past dietary habits must go into great detail (and must include such questions as to the occasional use of cashew and macadamia nuts, must bring out the differences between buttermilk, whole milk drinks, dried whole milk, evaporated milk, condensed milk, sweet or sour cream, and dried non-fat milk, evaporated skim milk, cream substitutes or the use of baked products known for their high animal fat composition, packaged dinners, desserts, etc.).

H. What Factors Enhance or Impede the Physician's Use of Diet Counseling Services? How May this Information be Used?

The physician's use of dietary counseling services depend on his personal interest and authority in the problems involved. If he does not personally attend to the details of a prescribed diet, he will not succeed. Those physicians who are willing to spend time in letting the dieticians participate in the medical and laboratory results of prescribed dietary changes will be most successful in the use of diet counseling services. This makes the dietician or nutritionist an active participant in the health delivery team rather than a passive bystander whose technical advice is being used occasionally without any responsibility for follow-up.

I. In What Roles can Personnel Other than Nutritionists be Used in the Dietary Programme? What Training Do They Need?

It is obvious that patients who have gone through a dietary programme themselves could be the best potential teachers for other patients. In

the past, we have used the experience of a physician's associate who for three months went through our programme and became a very good teacher to others; we have used the services of a registered nurse who, upon completion of her own dietary programme for severe hypertension was able to help us greatly in our diet instructions of other patients on a part-time basis. In the Hypertension Intervention Study in Evans County, Georgia (Heyden *et al.*, 1973) we have trained a housewife who had undergone the prescribed weight reduction and salt restriction, reduced her weight to a normal level and at the same time brought her hypertensive blood pressure levels under control. She subsequently observed our diet programme at the Department of Community Health Sciences for four days. Thereafter she successfully managed the weekly supervision of 63 obese, hypertensive individuals including detailed dietary advice about caloric values, fat content, the value of protein in low-caloric diets and the elimination of sodium rich foods. We feel that the training of a non-professional in a Nutrition Education Programme is best accomplished by having this particular person go through the programme herself and then supervising her on her instruction of patients, placing increased responsibilities into her hands. No formal education in nutrition or dietetics is required in our opinion.

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APPENDIX: POSSIBLE SIDE EFFECTS OF DIETARY FATS

A. Multiple Sclerosis

It is not surprising that many epidemiological hypotheses regarding multiple sclerosis, which still evades precise etiology, have been brought forward, tested and either disproved or left unproven. The incidence of this disease appears to be lower in warmer latitudes. It has been mentioned by several investigators that it is extremely difficult to study a low-incidence disorder like multiple sclerosis systematically. It is reported to occur more frequently in females, although this has not been found in all studies; in some studies there is an excess of males among older patients with multiple sclerosis. A viral etiology (Brody *et al.*, 1971) has been suspected as in many other chronic degenerative diseases. Even the type of tooth filling has come under suspicion. The disease supposedly occurs more frequently in higher socio-economic groups but proposed urban-rural differences in the incidence are not well documented (Bernsohn and Stephanides, 1967). The observation of a low familial occurrence is thought (not proven) to be associated with environmental rather than genetic factors. Another hypothesis concerns the epidemiological similarities between multiple sclerosis and Hodgkin's disease. The age of clinical onset is the same as in Hodgkin's disease. Newell (1970) also reported that the geographic distribution of mortality from multiple sclerosis in the United States is similar to the geographic distribution of Hodgkin's disease mortality among young adults in countries of the Western civilization. Both diseases are said to be rare in Japan.

A recent editorial in the *British Medical Journal* (6/5/71) mentioned the dietary hypothesis and listed several promoters of this theory. A few authors have drawn attention to the high incidence of multiple sclerosis in some parts of the world where diets generally tend to be rich in saturated fatty acids. In at least one retrospective study of patients with multiple sclerosis and control persons this hypothesis was not borne out.

The study of the dietary intake of non-hospitalized persons with multiple sclerosis by Witschi *et al.* (1970) revealed that the amount of total fat and the proportion of animal fat were lower than in studies of other investigators. Fat in the average daily diet of the male patients with multiple sclerosis ranged from 32-125 g (mean 73 g). Animal fat contributed 67% and 62% of the total fat for men and women respectively (19-109 g for men 19-93 g for women).

In comparison, Browe's (1967) group of healthy men (1514 civil service employees) showed a daily intake of 124 g of fat of which 74% was from

animal sources. In the study of Boston-Ireland brothers,* the dietary calculations of interviews from 85 pairs of brothers showed the Bostonians to have a mean fat intake of 158 g of which 86% was from animal sources. 70 dietary histories calculated by the Framingham study** showed an average fat intake of 154 g for men and 106 g for women, of which 75% came from animal sources. Davidson *et al.* (1962) obtained dietary records from 42 men and 62 women, all of whom were apparently healthy ageing persons and reported that animal fat provided over 70% of the total dietary fat for nearly three-quarters of the subjects. Studies of Benedictine monks, whose diet is comparable with that of the average American indicate that they derive 75% of their fat from animal sources.

It has been suggested that modification of the diet for patients with multiple sclerosis (reduction of total fat, inclusion of greater amounts of polyunsaturated fatty acids) may improve the patient's functional condition and reduce the relapse rate (Swank, 1961; Swank and Bourdillon, 1960). We agree with the editorial from the *British Medical Journal* that adding either sunflower seeds or corn oil to the normal diets of patients suffering from multiple sclerosis will do no harm. This eventually may turn out of importance to some patients, particularly in view of a more recent chemical investigation of the levels of linoleate and oleate levels of the serum lipids of patients suffering from multiple sclerosis and of controls (see Editorial, *Brit. Med. J.*, 1971). The percentage of linoleate in the patients with multiple sclerosis was lower than in the controls, while that of oleate was higher. The two groups of patients were then fed with linoleate supplements (emulsion of sunflower seed oil). In both groups the percentage of the linoleate levels rose strikingly, but it seemed to fall rather more rapidly in the patients with multiple sclerosis after termination of the dietary experiment. The low linoleate levels in multiple sclerosis patients are difficult to explain. Since the absorptive mechanism is unimpaired the suggestion was made that the rate of loss or of utilization of linoleate may be abnormally high in patients with multiple sclerosis.

In summary, the two facts, namely the diversity of etiological hypotheses in multiple sclerosis with contradictory statements from credible investigators and the—as yet unexplained but interesting—findings of an abnormally high utilization of linoleate or an abnormally high rate of loss of linoleate in patients with multiple sclerosis make it impractical to go beyond these speculations. However, it is felt that the dogmatic assertion that multiple sclerosis is the result of a dietary deficiency of polyunsaturated fatty acids is unwarranted at this time (see Bernsohn and Stephanides, 1967).

* Trulson *et al.* (1964). ** Mann *et al.* (1962).

B. Carcinogenesis

The question of undesirable side effects from the long-term use of a low-cholesterol diet with the emphasis on the polyunsaturated fatty acids briefly developed into a major public concern after the publication of an article in the *Lancet* on 3/6/71, "Incidence of cancer in man on a diet high on polyunsaturated fat" by Pearce and Dayton. In their eight-year controlled clinical trial of a diet high in polyunsaturated vegetable oils and low in saturated fat and cholesterol, 174 deaths were noted in the experimental group and 178 deaths in the control group. In the experimental group 31 of the 174 deaths were due to cancer as opposed to 17 out of 178 deaths in the control group. The authors unfortunately concluded from their findings that it is "premature to make a blanket prescription of a diet high in polyunsaturated fat for the entire population", implying that their data could mean that the polyunsaturated fatty acid diet might have had a co-carcinogenic effect in the experimental group. However, a review of the table showing adherence to diet in patients with fatal carcinomas during the diet phase clarifies the situation and removes any doubt that the diet high in polyunsaturated fatty acids and low in cholesterol might have had anything to do with carcinogenesis or co-carcinogenesis. Not less than 12 cases of fatal carcinoma were found in persons who adhered less than 20 % of the time to the experimental diet (see Table 7)

Table 7
Adherence to diet in patients with fatal carcinoma during the diet phase^a

Adherence(%)	Control group	Experimental group
0-10	2	10
10-20	1	2
20-30	1	3
30-40	0	0
40-50	3	3
50-60	3	3
60-70	0	4
70-80	2	2
80-90	4	1
90-100	1	3
	17	31

^a Adherence, calculated from attendance records, is expressed as a percentage of the maximum number of meals which could have been taken in the study dining-hall.

$\chi^2 = 10.26$; $P > 0.3$.

Only 19 persons from the experimental group, thus, died with cancer and adhered to the prescribed diet between 20 and 100 % during the eight year observation period. Therefore, any statistical significance is being automatically removed between the control and the experimental group since people in the experimental group who did not adhere to the diet can hardly be called dieters. It was, therefore, not surprising that another group of four investigators (Ederer *et al.*, 1971) found that the results of their studies "are consistent with the hypothesis that the cholesterol-lowering diets do not influence cancer risk".

C. Breast Cancer

In considering dietary fat intake and breast cancer, we are probably not even dealing tangentially with a causal relationship. Animal experiments in rats in the hands of one group of investigators (Carroll and Khor, 1971) showed that semi-synthetic diets containing 10 % and 20 % (by weight) of corn oil produced more mammary adenocarcinomas after treatment with a single oral dose of DMBA than in a group of rats on diets containing only 0.5 % or 5 % corn oil. The same investigators reported that experiments with ten different fats and oils fed at the 20 % level indicated that unsaturated fats enhance the yield of adenocarcinomas more than saturated fats. In addition, it was found that the diet high in corn oil enhanced the tumour yield when it was fed only after administration of the carcinogen but not when it was fed only before. This suggested to these authors that the effect was related to development of the tumours rather than to distribution and metabolism of the carcinogen or other factors concerned with tumour initiation. Reviewing other animal studies (Carroll and Khor, 1971), it appears that edible oils such as olive oil, Crisco and lard can enhance mammary carcinogenesis in the rat. The incidence of spontaneously occurring mammary tumours in rats was independent whether the fats were heat treated or untreated. The level of α -tocopherol was increased in another rat experiment containing 20 % corn oil and the result was a decrease in tumour yield in rats treated with DMBA.

Carroll and co-workers (1968) admitted that their findings with corn oil in animals did not support the epidemiologic observations by Lea. Lea had suggested that there was a positive correlation between consumptions of fats and oils and death rates from malignant neoplasm of the breast relating this to the cholesterol and cholesterogenic content of certain dietary fats. However, the example of the American black female with a definitely lower incidence of breast cancer in comparison to the white counterpart in the United States provides a good example of the irrelevance of this fat hypothesis in carcinogenesis of the breast. Black

females are known to have used in the past (and are still using at the present time) more animal fats in their diets than white females. There are more powerful environmental and sociological influences involved in the development of breast cancer than dietary factors, among others the age at first pregnancy, the number of pregnancies, cancer family history breast feeding versus non-breast feeding, the age at menarche, the age at menopause or artificial menopause, the presence or absence of benign cystic disease or treatment with oestrogen-containing hormones. For each one of the factors cited one can show great differences between white and black females and between Japanese women and American white females. The mortality from breast cancer is believed to be nine times higher among American whites than among Japanese women. However, environmental and sociological factors change drastically in Japanese immigrating to the United States west coast and Hawaii. With these changes, significant increases in breast cancer are being reported among first and second generation Japanese women.

Disregarding for the moment the isolated experimental finding of corn oil as co-carcinogenic in breast cancer development, one is more impressed by the several laboratory studies revealing that increasing the level of fat in general in the diet increases the yield of mammary tumours in laboratory animals. The higher incidence of spontaneous breast carcinoma in mice fed a high-fat diet has been reported as early as 1945. Other workers observed that rats develop more mammary fibroadenomas when fed on high-fat diets regardless of the type of fat used. On the other hand, there is ample evidence from animal experiments that underfeeding and caloric restriction decrease the incidence of a variety of tumours, including breast tumours. The literature on this subject has been summarized by Tannenbaum (1959).

However, this finding of an increase in breast cancer in overfed animals cannot be confirmed from human experience. Body weight and incidence of breast cancer cannot be correlated in available studies. The topic has been well reviewed in the German literature by Borneff and Fabian (1966) and by Schettler and Wagener (1965).

D. Colon Cancer

A report by the Research Committee of the World Health Organization (1966) assumed a positive association between the mortality from colon cancer and arteriosclerotic heart disease (ASHD). However, a negative correlation between the mortality from gastric and colon cancers suggested opposing etiological factors.

“The negative correlation of colon to gastric cancer, the positive association of colon cancer to arteriosclerotic heart disease and the

relatively high rate of colon cancer among Jews in New York City may be related to a dietary pattern, possibly high in terms of saturated fats. The low rate of colon cancer, particularly in Japan, is also consistent with this view." (Report of the Research Committee WHO on Gastroenterology, 1966.)

What does not fit into this apparent relationship between colon cancer and arteriosclerotic heart disease is the sex ratio of colon cancer. Rectum cancer is a predominantly male disease; however, in contrast, cancer of the colon generally has a slight predominance of women which of course is not true for ASHD in women in Western countries. Table 8

Table 8

Age-standardized rates^a of mortality from cancer of specified gastro-intestinal sites, at ages 0-74 years, for Japanese in Japan and Japanese and Caucasians in California

	Japan ^b		California ^c					
	(Japanese)		Foreign-born		U.S. born		Caucasian	
	Men	Women	Men	Women	Men	Women	Men	Women
Stomach (151)	58.4	30.9	29.9	13.0	11.7	11.3	8.0	4.0
Colon (153)	1.9	2.1	6.1	7.0	6.3	10.4	7.9	8.3
Rectum (154)	3.3	2.8	4.0	(4.0)	(3.1)	(2.0)	4.2	2.8
TOTAL (151, 153-4)	63.6	35.8	40.0	24.0	21.1	23.7	20.0	15.1

From Ackerman, 1972.

^a Age-standardized with direct method, using Segi's common standard as adopted by the working party of World Health Organization of Gastroenterology. See *Gut* 5, 196 (1964).

^b Average annual rates for 1960-61 in Japan.

^c Average annual rates for 1957-64 for Japanese in California and 1959-61 for Caucasians in California. Rates in parentheses are based on fewer than 10 deaths.

reflects the slightly higher age-standardized mortality rate for Caucasian women with colon cancer and a markedly lower mortality rate for Caucasian women with cancer of the rectum. The same applies to non-white females in the United States. It is important to keep this discrepancy in mind when one tries to interpret the marked decline of gastric cancer and sharp increase of colon cancer for American born Japanese, and Japanese living in California. Wynder and Shigematsu choose to interpret the increase of colonic cancer among the Japanese

migrants to the United States "a most important epidemiologic clue, that can best be accounted for by dietary changes" (Wynder and Shigematsu, 1967). These authors pointed out correctly (as was also shown by Ackerman, 1972: Table 8) that colon and rectum cancer is very rare in Japanese in their home country. In the Japanese diet only a small percentage of calories eaten is fat which is mostly polyunsaturated in contrast to 40-44% fat in the American diet, nearly half of which is saturated. Second generation Japanese in Hawaii also obtain about 40% of their calories from fat and their blood cholesterol levels are similar to those of the continental United States population. It is certainly tempting to correlate these two observations, the changes in the quality of dietary fat, the increase in total fat intake and the increase in colon cancer but proof is missing so far. Ackerman (1972) has contributed some laboratory observations to this hypothesis.

"Bacteriological studies of faeces in subjects from Britain and America have shown highly increased counts of bacteroides and a higher concentration of steroids than in Ugandans or Japanese. Furthermore, the steroids were degraded to potentially carcinogenic agents. We would expect a low fat vegetarian diet to be associated with reduced levels of neutral steroids and of bile salt degradation products in the faeces."

In the study just mentioned by Wynder and Shigematsu (1967) patients with colon cancer and control persons consumed eggs, milk, butter, cheese and meat in the same quantities. In three more studies no consistent relationships were found between cancer of the large bowel and fried food or milk consumption. Similarly, Pernu (1960) did not find any positive relationship between the development of cancer and animal meat and fat consumption. Higginson (1966) also reported no significant differences in any dietary intake between cases with cancer of the large bowel and control subjects.

After unsuccessful attempts to blame carcinogenesis of the colon on fats, recent research has turned to carbohydrates and roughage in the diet particularly after comparing data between South African Bantus and industrialized nations. The diet of the South African with his bulky stools and rapid transit is made up of high roughage and unrefined carbohydrates. The Western diet has low bulk with refined sugar and flours. This results in a longer transit time, decreased frequency of defaecation, faecal stasis and prolonged contact of any potential carcinogen with the mucosal surface (Ackerman, 1972 and Editorial-*Medical World News*, 1971). It may be relevant that most retrospective studies of patients with cancer of the colon and control persons revealed a

higher degree of constipation in the past history of the cancer patients. In contrast, the Bantu is obsessed with the idea that he must not be constipated. His concept of constipation differs from the Western concept. He feels that if he does not have three or four bowel movements per day he is already constipated and he remedies this situation by frequent enemas. The Bantu produces huge bulky stools and the faeces have a rapid transit. The rapid transit has been well documented by radiopaque markers and fluoroscopy (Ackerman, 1972). It would, therefore, seem appropriate to lay the fat hypothesis (as etiological factor in colon cancer) to rest.

Professor Rose (London) along with distinguished epidemiologists like Professors Keys, Blackburn, Taylor, Kannel, Paul and Reid as well as Professor Stamler recently published (Rose *et al.*, 1974) a study of 90 cases of colon cancer whose initial levels of blood-cholesterol were found surprisingly to be lower than expected. Rose and co-workers chose to interpret their data with the (I believe) unwarranted opinion that the patients with colon cancer were individuals with lower levels of blood cholesterol who tended to form more bile salts

“perhaps in part as a result of their higher intake of polyunsaturated fatty acids. This would increase the amount of substrate available for the carcinogen-forming bacteria, and hence increase also the risk of colon cancer. The negative association between blood cholesterol level and colon cancer risk might arise if in some individuals the intestine were more extensively colonised with bile-degrading bacteria, perhaps as a result of a higher intake of polyunsaturated fat or a lower intake of fibre. . . . There is need for further study of the relation in individuals between carcinogen producing faecal bacteria and the dietary intake of polyunsaturated fat and fibre.”

There is an uneasy feeling that this paper may have created the wrong impression that polyunsaturated fatty acids might be implicated in the development of colon cancer. Professor Rose kindly provided me with the actual number of patients who had their cholesterol determination within five years prior to death from colon cancer. As it turned out there were 48 patients, that is more than 50% of the total number of colon cancer patients, who died within five years of the cholesterol determination. In view of the importance of this question, we take a look at the five-year cancer survival rates published in the 1974 *Cancer Facts and Figures* of the American Cancer Society; we find colon and rectum cancer together. The five-year cancer survival rates are quoted as 69% in localized cases and 39% in cases with regional involvement. The chances to survive early diagnosis of colon cancer and surgery (and/or radiation therapy) are

pretty good. We therefore can assume that people dying within five years of their last cholesterol determination must have had either regional involvement or widespread metastatic disease.

The second question which I raised, was also answered by Professor Rose: 30 of the 90 individuals with colon cancer were 55 years and older. From the epidemiological literature it is a well-known observation that men above the age of 55 do have lower cholesterol levels or remain at a plateau compared to younger men whose cholesterol levels on the average rise from 180 mg % at 18 to 245 mg % at 50. Those 30 men in my opinion would have to be excluded from any further analysis of an

Table 9

Interval from screening to death (years)	No. of cases	% with cholesterol level "below expectation"
<2	13	77
2-3	20	60
4-5	15	53
6-7	11	82
8-9	5	40
>10	26	62
	—	—
	90	63
Age at screening (years)	No. of subjects	% with cholesterol level "below expectation"
<45	13	54
45-54	47	70
55-64	27	59
>65	3	67
	—	—
	90	63

Note: in none of the 90 patients was even an attempt made to assess retrospectively the consumption of polyunsaturated fats and oils.

alleged association between low cholesterol and development of cancer of the colon. Professor Rose in a personal communication added that

"the cholesterol deviation to lower levels is greater when the interval from screening to diagnosis is short, i.e. in sick men. If we take out the men found within one year to have cancer, there is not in the remainder any correlation between cholesterol deviation and interval to diagnosis."

An editorial of the *British Medical Journal* (1973) came to the conclusion "No convincing case has been made that PUFA cause either premature ageing or cancer". A recent study, presenting the 13-year experience of the Diet and Heart Disease Study conducted by Singman *et al.* (1973), similarly concluded: "Our observations lend no confirmation to the alleged association between excess cancer mortality and high PUFA diets". This study was mentioned earlier. In brief, 1764 men, 40–59 years of age, have come under long-term observation: a control group of 533 men, an active experimental group of 378 men keeping a relatively high PUFA diet and an inactive experimental group of 853 men who were once active subjects but now limit their participation to appearance at the study facilities annually for physical examination to ascertain the status of study end-points were also included. The results of the 13-year observation period are presented in Table 10.

Table 10
Number of deaths in study group, by cause as of September 1970

Cause	Experimental		Control
	Active	Inactive	
Heart disease ^a	30	58	10
Cancer	6	15	10
Other	5	12	5
Total	42	85	25
Person-years of observation	5903	6156	4372

^a Includes the group of subjects who entered the study with prior overt coronary heart disease. These subjects have never been included in prior reports since they could not add to the experience concerning new coronary heart disease. However, they have been included here since they can contribute to cancer experience (Singman *et al.*, 1973).

Regarding the specific question raised by Rose and co-workers, the following table (Table 11) does not lend support to the hypothesis advanced by Rose *et al.*

Obviously, the lowest number of deaths from cancer was encountered in the active experimental group with only one case of colon cancer! Table 12 reveals the expected and actual number of deaths from cancer. In the age group 40–49 years not a single case of cancer was observed

Table 11

Number of deaths in study group from cancer, June 1957 to September 1970

Site	Experimental		Control
	Active	Inactive	
Esophagus	1		
Stomach			3
Colon	1	3	1
Rectum		1	
Pancreas	1	1	
Liver		1	1
Larynx		1	
Lung	1	3	1
Prostate		1	
Spine	1		
Brain	1	1	1
Lymphosarcoma		2	2
Leukemia			1
General peritoneal		1	
Total	6	15	10

^a Cases of cancer in inactive subjects developing within six months of becoming inactive have been charged to the active group (Singman *et al.*, 1973).

Table 12

Expected and actual number of deaths from cancer

Group	Age at entry to study group			
	40-49		50-59	
	Observed	Expected	Observed	Expected
Experimental				
Active	0	1.6	6	23.3
Inactive	0	3.1	15	19.7
Total	0	4.7	21	43.0
Control	2	3.6	8	13.2

From Singman *et al.* (1973).

in the active or inactive experimental group; however in the age group 50–59 years the observed deaths from cancer in the active experimental group was four times lower than expected. In the inactive experimental group and in the control group the observed deaths from cancer were much closer to the expected number of deaths. The evidence thus presented exculpates polyunsaturated fatty acid diets from causing cancer.

E. Gastric Cancer

At present it is safe to state that any evidence, from animal experiments and from a few retrospective studies of human cancer patients, for cancer induction by dietary fats is of purely academic interest.

O'Gara *et al.* (1969) concluded from animal studies that "corn oil appears to contain either more of the carcinogen or a more potent one than hydrogenated fat". He therefore suggested that it would be "advisable to avoid the excessive re-use of cooking fats in the preparation of foods for human consumption". On the other hand, two retrospective studies of stomach cancer patients and controls did not show any difference in the use of fat. Graham *et al.* (1967) applied the questionnaire method to 188 males with cancer of the stomach and 800 control patients without neoplastic diseases and found no significant differences in the type of fats used for frying. Higginson (1966) stated that patients with gastric cancer showed a dietary pattern indicating an increased use of animal fats, cooked fats, fried foods, bacon, and a decreased use of dairy products in comparison to control persons. However, the differences between patients and controls were not statistically significant. Gastric cancer patients had a slight increase in daily use of pork, sausage and bacon, and a slightly increased consumption of fried potatoes, fried foods for breakfast and fried meats. Furthermore, in patients with gastric cancer a modestly increased use of lard and collected fats was demonstrated. They used predominantly animal fat in cooking as compared to the controls. A higher proportion also re-used their fats but the answers were open to doubt because a social stigma is attached to re-use of fat. Higginson concluded that the degree of increased use of homemade lard, bacon drippings, collected fats and/or of reduced use of refrigeration among the gastric cancer patients was insufficient to support a causal relationship between fat and gastric cancer.

"Thus, while heated or animal fats would appear unlikely as major carcinogenic or co-carcinogenic agents in gastric carcinoma, our findings would suggest that they cannot be completely excluded as

of etiological significance, since they are widespread dietary items in many communities with a high frequency of gastric carcinoma."

Evidence from both animal experiments and from the retrospective studies just quoted would, however, not pertain to the findings in Japan where there is the highest stomach cancer morbidity and mortality in the world. The diet of the Japanese is known to be low in fat and the majority of the fat stems from vegetable oils. Even more important are the rapidly changing age standardized rates of mortality from gastric cancer in Japanese men and women moving to Hawaii and the west coast of the United States. As can be seen in Table 8 (p. 101), stomach cancer mortality decreases almost by half in the foreign born Japanese living in Hawaii and the United States and a further decline occurs in American born Japanese approximating the rates of the host country.

An interesting hypothesis has been advanced by Stukonis and Doll (1969). They confirmed the well known relationship between gastric cancer and low social class in England. In their hypothesis, they went one step further and compared the physical activity and caloric expenditure at work of men in low and high social groups. They found that a banker, for example, would expend only 2850 kCal per day whereas a miner may expend as many as 4030 kCal per day.

"Men, whose work involved expenditure of a large amount of physical activity, require to consume more food and, if carcinogens in foods are responsible for the production of gastric cancer, men who eat more will be more at risk for developing the disease. The mean calorie intake of housewives (2100 kCal) was lower than that for any of the groups of employed males and it is possible that differences in the amount of food eaten could be largely responsible for the fact that the incidence of gastric cancer is almost universally 50 to 100% higher in men than in women."

The authors concluded that differences in dietary habits between men in different social classes were likely to be important. Among them, carcinogens may be present in greater concentration in cheap foods than in expensive foods. However, no detailed analysis was made in the amount of fat consumed in these two groups. The standardized mortality ratio for gastric cancer for men in England (1949-53) in occupations requiring light physical activity was 84, in occupations requiring intermediate activity 106 and in occupations requiring heavy physical activity 147.

Wynder and Shigematsu (1967) mentioned that death rates for colon cancer have a strong negative correlation with those of gastric cancer. A negative correlation was also found between gastric cancer mortality and arteriosclerotic heart disease mortality.

F. Cholelithiasis

The so-called AHA- (American Heart Association) diet, or Prudent Diet or PUFA-Diet has produced some unexpected side effects. For example, the effect of long-term ingestion of a diet low in cholesterol and saturated fat, and high in unsaturated fat on cholelithiasis has been evaluated. Autopsy records from the Los Angeles Veterans Administration clinical trial on the prevention of coronary heart disease were reviewed (Sturdevant *et al.*, 1972). Subjects in the trial were male veterans over 54 years old. During the eight-year study, 351 deaths occurred; 187 autopsy records were classifiable for presence or absence of gallstones. Stones were found in 23 out of 92 (25%) of autopsied subjects who had eaten the experimental diet, and in 14 out of 92 (15%) autopsied subjects who had eaten the control diet ($P = 0.12$). Stratification on adherence to diet with elimination of the lowest-adhering third showed that 20 out of 61 (33%) experimental subjects and 9 out of 64 (14%) controls had stones ($P = 0.02$). Of those who ate more than 500 meals during the study, 19 out of 63 (30%) experimental subjects and 11 out of 70 (16%) controls had stones ($P = 0.08$).

Mean weight at entry to study was significantly greater in subjects with gallstones at autopsy:

	Weight of men with gallstones	Weight of men without gallstones	<i>P</i>
Experimental	75 kg (165 lb)	67 kg (147 lb)	0.01
Control	77 kg (169 lb)	69 kg (152 lb)	0.02

Of those subjects who were more than 15% over desirable weight, 15 out of 49 (31%) had stones, as did 22 out of 136 (16%) of the non-obese subjects ($P = 0.06$). The authors specifically stated that weight loss was not related to the finding of gallstones. In addition, only very few persons lost any appreciable amount of weight.

“Mean serum cholesterol at entry, and mean change in serum cholesterol during the study, were not related to presence or absence of stones.”

“These data suggest that long-term consistent ingestion of the experimental diet predisposed to gallstone formation in these men. An adequate biochemical explanation of this hypothesis is not available. Population studies of prevention of atherosclerosis by similar diets should include investigations of cholelithiasis.”

This reviewer still feels that the weight of an individual and the degree of obesity may be a more important factor than dietary fatty acid composition. Unfortunately, the gallstones were not analysed. This would have been interesting in the light of animal experiments (Dam, 1971), showing that the incorporation of soyabean oil and cod liver oil in the diet increases the tendency to produce amorphous pigmented gallstones. On the other hand (also in animals), fats containing polyunsaturated fatty acids counteract the formation of cholesterol gallstones! The same author demonstrated the difference in the effects of a butter fat diet and a diet of 40 % linoleic acid containing margarine: with butter fat, 60 % of the animals had cholesterol gallstones, whereas with the margarine diet only 4.6 % had cholesterol gallstones. The incidence of amorphous pigmented gallstones was low with both types of fat.

G. Unexplained Effects on Blood Pressure, Cigarette Smoking and Uric Acid Concentration

Drastic dietary changes are followed by unexplained effects on several parameters. In the National Diet-Heart Study, the emphasis was on lowering serum cholesterol concentrations but blood pressure was also found to be lower than prior to the trial. In addition, cigarette smoking habits changed since more people had quit smoking cigarettes at the end of the two-year trial in comparison to those who had started smoking cigarettes during these two years of observation. Rinzler (1968) reported from the Anti-Coronary Club that among persons adhering to the so-called Prudent Diet, the percentage of hypertensives was decreased within four years, from 25.9 % to 9.9 %, in contrast to control persons where the percentage of hypertensives increased from 10.9 % to 13.1 % within the same time. In this particular study, cigarette smoking did not change significantly in the experimental group. In a study of 59 non-obese, normal and hyperlipidaemic men, reported by Wilson *et al.* (1971), adherence to the American Heart Association diet produced, within six months, a slight increase of uric acid values. All mean values during the diet period were higher than baseline values. The difference between baseline and the peak value was statistically significant. Only a minor difference between the weight at the intake examination and at the end of this six months observation period was noted (minus 0.6 kg: 1.4 lb). No significant change was noted in systolic and diastolic blood pressure during these six months.

Obviously, the unexplained effects of dietary changes on several parameters should be studied more systematically. It is evident that we must differentiate the effect of dietary changes in initially overweight and initially normal weight subjects.

CONCLUSIONS

From the material presented, several conclusions seem to be justified.

1. Any association, alleged to exist between the use of polyunsaturated fatty acid and the development of cancer in several organs can be dismissed. Evidence brought forward in favour of this hypothesis has been examined and evidence contrary to the assumed relationship has been presented.

2. The relationship between polyunsaturated fatty acids and multiple sclerosis needs further evaluation. The correlation found between dietary fat intake and the disease under study may be purely circumstantial but it is felt that it is definitely worthwhile to pursue the hypothesis further in larger groups of patients, both in retrospective studies of dietary habits of patients and controls and as therapy in comparison to a group of patients treated without any dietary intervention.

3. The advantage shown in several prospective studies of a diet low in cholesterol, high in polyunsaturated fatty acid for the prevention of major coronary events and the prevention of recurrence of myocardial infarction and death from myocardial infarction is substantial. Beneficial effects of such a dietary regime have been shown in all trials with the notable exception of the investigations reported from the United Kingdom. Reasons for this discrepancy are not clear. On the other hand, it seems inescapable that all these studies have been started with subjects at a rather late age, resulting in a definite decrease of atherosclerotic heart disease but not altering the overall mortality in the post-dietary phase of several trials. An increasing number of investigators in the field of atherosclerosis research feel that the whole question of development of the disease, and prevention of it, is a pediatric problem and we, therefore, may only see a major impact on this epidemic by starting dietary intervention at school age. Recognition of this important aspect and actual institution of dietary changes on a population-wide basis may take several years. In the meantime, we are faced with the problem of changing dietary habits among the adolescent and middle-aged population in Western countries who need to be educated, persuaded and motivated to accept the dietary changes on a life-long basis.

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COMMENT ON GOAL 5

(Only in reference to p. 46 statement on caffeine)

In view of the unwarranted allegations against coffee and caffeine it seems to be necessary to repeat the same negative findings about coffee consumption and health which have been published from several prospective studies. We had our latest report from the Evans County Heart Research in Claxton, Georgia.

LITERATURE

Heyden, S.; Tyroler, H. S.; Cassel, J. C.; Hames, C. G.; Becker, C. and Heiss, G.: Coffee Consumption and Mortality in a Community Study—Evans Co., Ga. *Z. Ernährungswiss.* 15:143, 1976.

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Coffee consumption and mortality in a community study — Evans Co., Ga.*)

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With 1 figure and 3 tables

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Introduction

In view of the ongoing debate about whether coffee drinking influences the development of myocardial infarction, we have identified the following points which might contribute to the clarification of this issue. 1) It appeared advantageous to study *coffee drinking habits among all residents of a total community* rather than to rely on answers to questionnaires in hospitalized patients or other selected sub-groups of the population. 2) In addition, benefits were expected from a *prospective study*, i.e. to define disease free cohorts exposed and not exposed to coffee to be followed over a certain period of time. To record the coffee-drinking habit in a retrospective fashion – after the disease has appeared – may give misleading results in view of the vague recall and changing coffee drinking patterns after a clinical event. 3) Furthermore, it is obviously of value to keep the *observation period (after recording the coffee drinking habits) as short as possible* since it cannot be assumed that individual coffee-drinking habits remain stable over long periods.

Methods

These requirements were met by the long-term epidemiological study carried out in the Southeastern part of the United States, the Evans County Study in Georgia. 1) The prevalence survey in this community was conducted in 1960–62 and the study population re-examined between 1967 and 1969. 2) At this second study of 2,530 adults (60% white, 40% black) the two examining physicians asked each person a few standardized questions concerning coffee consumption. Persons who gave a history of regularly drinking five cups of coffee or more per day were placed in the high coffee consuming group. All others were classified as low- or no coffee consumers. 3) The cohort was followed for a period of four and one-half years

*) Vortrag auf dem VII. Internat. Wissenschaftl. Kolloquium über Kaffee, Hamburg 1975.

with annual questionnaires. 4) Between Juli 31, 1969 and January 1, 1974 a total of 339 deaths occurred. Completeness of follow-up was practically assured through the annual interviews, since each person was contacted either personally or by telephone on the date of his examination anniversary. This interview covered questions of intercurrent illnesses, doctor visits, medications and hospitalizations. Ascertainment of death was monitored in several ways. Regular searches were conducted at the hospitals used by this community, the death certificates accumulated in the Evans County Courthouse were reviewed periodically, the local obituary columns were screened daily, and the funeral homes contacted at regular intervals. Early in 1975 the Georgia Department of Health was asked to assist in the search of deaths which had occurred among Evans County residents outside of Evans County. A comparison of the records showed completeness in the ascertainment of deaths.

This report comprises deaths which have occurred over a four and one-half year observation period. Of 339 deaths, 130 (38%) were confidently attributed to cardio- and cerebrovascular causes. They were confirmed by autopsy reports, hospital records, reviews by a neurologist and by a cardiologist of all available information including family and/or co-workers interviews in cases of sudden death. "Possible" cardio- and cerebrovascular deaths were classified together with all other causes of death, e.g. accidents, post-operative complications, pneumonia or cancer. The indirect method was used for age adjustment within each race sex group.

The choice of mortality as the end-point for this study was made because our cross-sectional study in 1967-69, analyzing coffee drinking in relation to coronary heart disease and stroke, had not revealed any difference in high coffee or low coffee consuming groups (1). At that time we pointed out the disadvantage of the study: by questioning a population about certain habits and correlating the answers with findings from physical examinations, laboratory studies, Ecg, etc., one automatically limits the study to survivors of the diseases under consideration. One of the manifestations of ischemic heart disease, death from myocardial infarction, sudden death and stroke death thus escape a cross-sectional study. If it were assumed that the heavy coffee drinkers all had died from ischemic heart disease or stroke prior to our survey in 1967-69, we would indeed have missed these important aspects of CHD and cerebrovascular disease (CVD).

Results

The results are best summarized in the following statements:

- a) *Mortality from all causes in this total community is not significantly different for white males (WM), white females (WF), nor black males (BM) among those who gave a history of high coffee consumption (≥ 5 cups/day) and those who drank little or no coffee. There is a suggestion of lower total mortality among black females who drink 5 + cups. However, despite statistical significance, this result must be considered tentative because of small numbers. Therefore, total mortality is not influenced by the coffee drinking habit - if anything, the group*

Tab. 1. Risk of Mortality from All Causes, by Coffee Drinking, Race and Sex Rates (%) Adjusted for Age and Smoking Habits*)
Evans County Cardiovascular Survey

Race/Sex		Daily Coffee Consumption		Adjusted Rates (p)
		< 5 Cups	5 + Cups	
White Males	PAR/Cases	556/72	94/10	
	Adj. Rates	12.95	11.29	NS
	S.M.R.	1.00	0.87	
	Approx. S.E. of S.M.R.	0.11	0.27	
White Females	PAR/Cases	639/53	134/9	
	Adj. Rates	8.29	8.91	NS
	S.M.R.	1.00	1.07	
	Approx. S.E. of S.M.R.	0.14	0.36	
Black Males	PAR/Cases	323/53	18/3	
	Adj. Rates	16.41	19.81	NS
	S.M.R.	1.00	1.21	
	Approx. S.E. of S.M.R.	0.14	0.70	
Black Females	PAR/Cases	427/52	32/1	
	Adj. Rates	12.18	3.65	.02
	S.M.R.	1.00	0.30	
	Approx. S.E. of S.M.R.	0.14	0.30	

*) Indirect Method

of high coffee consumers appears slightly favored by a lower mortality in comparison to persons with low- or no coffee intake (tab. 1).

- b) *Mortality from cerebrovascular disease (CVD) showed statistically significant differences among the two coffee drinking groups.* Whereas stroke deaths were found more often in white males (WM) and black males (BM) who had reported low or no coffee consumption during lifetime, white females (WF) and black females (BF) had somewhat higher age-adjusted stroke mortality rates among heavy coffee consumers than among the low- or no coffee drinking counterpart. Attention once more, however, is called to small sample sizes. There is however no suggestion of a deleterious effect attributable to coffee drinking (tab. 2).
- c) *Mortality from coronary heart disease (CHD) did not show any statistically significant difference between the heavy coffee drinkers and the low- or no coffee drinking persons in three out of four race-sex groups.* WM in the five-cup-of-coffee (+) group had a slightly higher CHD mortality rate. WF in the five-cup-a-day group had a marginally lower CHD mortality than WF who did not indulge in the coffee drinking habit. CHD mortality rates for Blacks, though statistically significantly

Tab. 2. Risk of Mortality from Stroke, by Coffee Drinking, Race and Sex
Rates (%) Adjusted for Age*)
Evans County Cardiovascular Survey

Race/Sex		Daily Coffee Consumption		Adjusted Rates (p)
		< 5 Cups	5 + Cups	
White Males	PAR/Cases	608/13	102/0	0.00
	Adj. Rates	2.14	0	
	S.M.R.	1.00	0	
	Approx. S.E. of S.M.R.	0.27	—	
White Females	PAR/Cases	673/4	136/4	NS
	Adj. Rates	0.59	3.89	
	S.M.R.	1.00	6.55	
	Approx. S.E. of S.M.R.	0.50	3.27	
Black Males	PAR/Cases	334/9	18/0	0.00
	Adj. Rates	2.69	0	
	S.M.R.	1.00	0	
	Approx. S.E. of S.M.R.	0.33	—	
Black Females	PAR/Cases	446/7	32/1	NS
	Adj. Rates	1.57	8.43	
	S.M.R.	1.00	5.37	
	Approx. S.E. of S.M.R.	0.38	5.37	

*) Indirect Method

higher for those with low coffee consumption can not be seriously considered due to a small number of black high coffee consumers (tab. 3).

- d) Inconsistencies in the frequency of higher and lower vascular mortality rates among the four race-sex groups, with diverging trends in statistical significance, led us to the conclusion that there is no relationship between coffee drinking habits and mortality from either all causes or from specific vascular diseases. *If one were to assume a higher CHD death rate among heavy coffee drinkers, one would have to explain a "protective" effect of coffee from other causes of death since all causes of death (total mortality) were equally distributed between high coffee and low- or no coffee consumers in our study (tab. 1).*
- e) Our rigid criteria for the diagnosis of death due to CHD or stroke (see methodology section) might have inflated the category "other causes of death" somewhat. Thus, the theoretical possibility exists that we may have misplaced a CHD death in the "mortality from other causes" category. Chances are that this rare instance could have occurred among the lower socio-economic group with less documentation by either Ecg, hospital records or autopsy reports, in which case a death

due to CHD would have been lost from the CHD group and would have entered the "other causes of mortality" group. However it is not our impression that, in general, higher coffee consumption is found more frequently among the upper socio-economic group. Therefore, if this instance of misplacing a CHD-death has occurred, it would mean a case of CHD death was lost from the low- or no coffee consuming group.

Discussion

An era of intensive search into potentially dangerous properties of caffeine and/or coffee on human health has produced a large volume of articles over the past decade. Gout, hypertension, diabetes, hyperlipidemias were all at one time alleged to be associated with a detrimental effect of high coffee intake. Most of the proposed coffee-associated effects were dismissed on the basis of clinical, epidemiological and experimental studies. Two issues remained to be solved in that reports indicated that ischemic heart disease, and peptic ulcer were associated with a high coffee intake.

Tab. 3 a. Risk of Mortality from CHD, by Coffee Drinking, Race and Sex
Rates (%) Adjusted for Age*)

Evans County Cardiovascular Survey

Race/Sex		Daily Coffee Consumption		Adjusted Rates (p)
		< 5 Cups	5 + Cups	
White Males	PAR/Cases	575/13	96/4	NS
	Adj. Rates	2.26	4.53	
	S.M.R.	1.00	2.00	
	Approx. S.E. of S.M.R.	0.28	1.00	
White Females	PAR/Cases	646/10	138/1	NS
	Adj. Rates	1.55	0.97	
	S.M.R.	1.00	0.63	
	Approx. S.E. of S.M.R.	0.32	0.63	
Black Males	PAR/Cases	337/4	19/0	0.03
	Adj. Rates	1.19	0	
	S.M.R.	1.00	0	
	Approx. S.E. of S.M.R.	0.50	-	
Black Females	PAR/Cases	441/4	34/0	0.04
	Adj. Rates	0.91	0	
	S.M.R.	1.00	0	
	Approx. S.E. of S.M.R.	0.50	-	

*) Indirect Method

Tab. 3 b. Risk of Mortality from CHD, by Coffee Drinking, Race and Sex Rates (%) Adjusted for Age and Smoking Habits*)

Evans County Cardiovascular Survey

Race/Sex		Daily Coffee Consumption		Adjusted Rates (p)
		< 5 Cups	5 + Cups	
White Males	PAR/Cases	575/13	96/4	NS
	Adj. Rates	2.26	4.94	
	S.M.R.	1.00	2.18	
	Approx. S.E. of S.M.R.	0.27	1.09	
White Females	PAR/Cases	646/10	138/1	NS
	Adj. Rates	1.55	1.03	
	S.M.R.	1.00	0.67	
	Approx. S.E. of S.M.R.	0.32	0.67	
Black Males	PAR/Cases	337/4	19/0	0.03
	Adj. Rates	1.19	0	
	S.M.R.	1.00	0	
	Approx. S.E. of S.M.R.	0.50	-	
Black Females	PAR/Cases	441/4	34/0	0.04
	Adj. Rates	0.91	0	
	S.M.R.	1.00	0	
	Approx. S.E. of S.M.R.	0.50	-	

*) Indirect Method

1. The prospective *Framingham* Study (2) and the 1967-69 cross-sectional study in Evans County (1) did not demonstrate an increase in any of the common risk factors predisposing to ischemic heart disease among heavy coffee drinkers with the exception of cigarette smoking. Cigarette smoking was strongly correlated with heavy coffee consumption. If there was a higher CHD incidence among heavy coffee drinkers compared to no- or low-coffee consumers it could be explained on the basis of the strong correlation between the two habits, as shown earlier from the Chicago electrical workers study (3). The *Framingham* (2) - as well as the Chicago Western Electric Study (3) and the *Kaiser Permanente* Study (4) refuted an association between heavy coffee consumption, per se, and the incidence of myocardial infarction or death from ischemic heart disease. The present 4½-year mortality study from Evans County taking coffee drinking habits into consideration and adjusting for age (even without controlling for cigarette smoking), showed no statistically significant differences in CHD deaths among heavy and no- or low-coffee drinkers. These findings are in contrast to retrospective studies of hospitalized patients with myocardial infarction and a control group hospitalized for

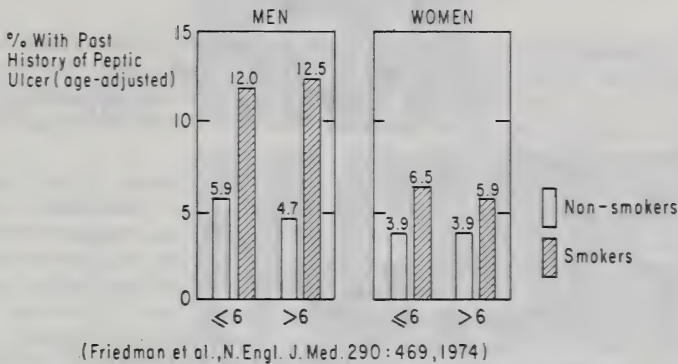


Fig. 1 (see text).

a variety of diseases (5), particularly cancer, there we would expect the condition to affect the exposure.

2. The widely held opinion that peptic ulcer may be caused by high coffee consumption was challenged recently by the Kaiser Permanente Group study (6) (1974) in California. 2,597 patients with peptic ulcer were questioned about their coffee drinking and cigarette smoking habits. Coffee drinkers of six cups and more did not have a higher prevalence of peptic ulcer than persons who drank less than six cups/day. On the other hand, there is no association with coffee drinking habits since *non-smoking* high or low coffee consumers in both sexes practically have the same low prevalence of peptic ulcer. A highly significant difference exists only among smokers and non-smokers, regardless of whether they drink much or very little coffee (fig. 1).

Summary

Total mortality showed no association with heavy coffee consumption in the four race-sex groups of Evans County. Deaths from coronary heart disease in WM, WF and BM showed no statistically significant differences between the two coffee consuming groups. Sex differences in cerebrovascular death rates, consistent in both races, suggest the possibility for a female excess of stroke deaths among coffee drinkers, and a "protective" effect of coffee drinking among males. Thus, in an area of the United States which has been designated the "Stroke Belt", neither the cardiovascular nor the cerebrovascular death rates seem strongly nor consistently related to coffee drinking habits.

Although the number of deaths (339) is fairly large, representing a 13% mortality in this community over a four and one-half year observation period, the classification in four race-sex groups with further division into the groups with different coffee drinking habits limits each stratum to rather small numbers. In addition, 86 cases of CHD and CVD were diagnosed during lifetime already and, therefore, were excluded from the prospective mortality study. Confidently to refute or confirm the allegations of a detrimental influence of high coffee intake on ischemic heart disease one would need larger numbers. But in the light of our most important finding – that mortality from all causes is not increased in the high coffee consuming group – the finding of increased ischemic heart disease death rates with high coffee consumption would have to be compensated by a provocative, lower rate for other causes of death.

Zusammenfassung

1. Die Gesamtsterblichkeit an allen Todesursachen ist gleichmäßig auf starke und schwache Kaffeekonsumenten verteilt. Tab. 1 zeigt sogar, daß die Kaffeetrinker von 5 Tassen und mehr pro Tag unter den weißen Männern eine etwas niedrigere Sterblichkeit an allen Todesursachen haben als die wenig oder nicht Kaffee trinkenden Personen.

2. Die Apoplexie-Mortalität zeigte in diesen 4½ Jahren divergierende und schwer erklärliche Unterschiede in den vier Geschlechts- und Rasse-Untergruppen. Während weiße Männer und Neger (die die höchste Apoplexierate in diesem Teil der USA zu verzeichnen haben) in der starken Kaffeekonsumgruppe keinen einzigen Fall von Zerebralinfarkt oder Gehirnblutung hatten und in der wenig oder keinen Kaffee trinkenden Gruppe 2,8% bzw. 3,2% mit tödlicher Apoplexie gefunden wurden, bot das weibliche Geschlecht ein anderes Ergebnis: Weiße Frauen und Negerinnen mit Kaffeetrinkgewohnheiten von 5 Tassen und mehr pro Tag hatten ein höheres Apoplexierisiko als die wenig Kaffee trinkenden Frauen.

3. Die Myokardinfarkt-Mortalität zeigte keine statistisch signifikanten Unterschiede zwischen starken und schwachen Kaffeetrinkern in allen vier Untergruppen, nachdem die Altersberichtigung durchgeführt und die Rauchgewohnheiten mitkontrolliert wurden.

4. Die Tatsache, daß die am meisten für Apoplexie gefährdete Gruppe von Männern im Südosten der USA unter starken Kaffeetrinkern keinen Todesfall aufwies, sowie die statistisch nicht signifikanten Unterschiede in der Myokardinfarkt-Sterblichkeit zwischen stark oder wenig Kaffee trinkenden Personen in dieser prospektiven Studie, und vor allem die leicht erhöhte Gesamtsterblichkeit an allen Todesursachen bei den wenig oder keinen Kaffee trinkenden weißen Männern, stellt u. E. alle Spekulationen über einen krankheitsfördernden Einfluß des Kaffees in Frage.

5. Obwohl die Zahl der Todesfälle ($n = 339$) ziemlich groß ist, d. h. 13% Mortalität in dieser Gemeinde innerhalb von 4½ Jahren, ist die statistische Analyse erschwert durch vier Geschlechts- und Rassegruppen mit weiterer Unterteilung in 2 Kaffee-Konsumgruppen. Um die Behauptungen über schädliche Auswirkungen eines hohen Kaffee-Verbrauchs auf das Myokard oder die Koronargefäße zu widerlegen, mußte man mit noch größerem Zahlenmaterial arbeiten. Aber im Hinblick auf unseren wichtigsten Befund – daß die Sterblichkeit an allen Todesursachen unter starken Kaffeetrinkern nicht erhöht ist – erlauben wir uns die Ansicht, daß weitere Untersuchungen zu diesem Thema eine unfruchtbare Zeitverschwendung darstellen.

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RISK FACTORS OF ISCHEMIC HEART DISEASE

Risk Factors of Ischemic Heart Disease

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Foreword

According to the Statistical Year-Book of the German Federal Republic, in 1973 145,000 persons died of cancer, 125,000 of ischemic heart disease, 108,000 of cerebrovascular disease, 18,500 of diabetes and its sequelae and 13,000 of chronic hypertensive disease.

This is a further increase of causes of death which originate in the vascular system and metabolism – quite in contrast to the year 1948, when only 2,600 deaths from ischemic heart disease were recorded.

Recent advances in epidemiology have clarified some of the etilogic factors. An increasing trend of degenerative heart and vascular diseases as well as diseases of metabolism is seen worldwide. However, this trend is not observed in those developing countries whose populations exist on calorically inadequate diets. With Westernization and acculturation to the living standard of industrialized societies, an increment of degenerative cardiovascular diseases takes place in these populations. These changes parallel those witnessed in Germany after the end of food rationing. Recognition and further research into the risk factors for the development of ischemic heart disease have produced strong evidence that risk factors cause and enhance disease development.

Professor Siegfried HEYDEN presents a synopsis of the available data. He uses facts, discussing them both critically and with a high degree of competence. This synopsis is the basis for preventive actions in the general practitioner's office. From the public health standpoint this book deserves great attention because it shows ways for prevention, intervention and rehabilitation in cardiovascular diseases. According to a study by EPSTEIN (1973) on 1,000 middle-aged males, approx. 10% will suffer from myocardial infarction within the subsequent 10 years. At least $\frac{1}{4}$ of those myocardial infarcts will manifest themselves as sudden deaths, e. g. at least 25 men will die within an hour. The remaining 75 are expected to reach the hospital; however, $\frac{1}{3}$ are apt to die within the next 4 weeks as will be shown in one of the following chapters (Commentary). Risk factors which contribute to myocardial infarction, are found in $\frac{2}{3}$ of cases – risk factors defined as hypercholesterolemia, hypertension and cigarette smoking. In world-wide studies it was demonstrated that risk factors develop during youth and adolescence. Within a few years they affect the vascular sy-

stem and several target organs. There are remarkable similarities between risk factors which may cause or enhance the progression towards myocardial and cerebral infarction as well as peripheral vascular disease. Medical research is now concentrating on causes of death in young and middle-aged persons. Research into the combination of risk factors assumes a rather important role. Every one of us is at potential risk and it is mandatory to search for the well-known risk factors in each individual, in the potential patient and in those who have already sustained myocardial infarction. This, then, becomes an obligation of the practicing physicians. It was the intention of Prof. HEYDEN to dedicate this brochure to them. I am sure it will be received with great interest by physicians of all specialties.

G. SCHETTLER, Heidelberg

Introduction

One of the goals of preventive cardiology is the discovery of the patient who is at risk for ischemic heart disease. The clinical observation, in the majority of cases, comes after the disease has manifested itself. Traditional tools of clinical diagnosis are able to confirm the presence of the disease only after it is relatively far advanced. Neither with the stethoscope nor percussion, neither with the chest X-ray nor with the usual questionnaire for the past history, in many cases not even with the resting ECG are we able to diagnose subclinical coronary artery disease. On the basis of coronary angiography, it is difficult to believe that at this late stage drug therapy or a physical activity program will change or influence the further course of the disease. The experiments with animals in the opinion of STUDER and REBER (1963) have not proven applicable to human atherosclerosis. New means of research had to be introduced after the animal experiment and the classic bedside observation of the patient did not yield practical pointers for early detection and intervention. The means emerged from two decades of epidemiologic prospective examinations of defined populations. *Epidemiology has revealed a third dimension in the research of ischemic heart disease. The application of results from epidemiologic research has provided the methodology and rationale for measures of intervention and treatment of risk factors.* No single animal experiment and almost no clinical observation after myocardial infarction would have enabled us to develop a program for early detection, i. e. screening for risk factors.

Framingham was a mile stone in the history of American medicine. Examination of adult men and women aged 30–59 years started in 1949 – at a time when infectious diseases as major causes of morbidity and mortality were being replaced by epidemic chronic-degenerative cardiovascular diseases and diseases of metabolism.

The post-Framingham era (arbitrarily set after 1970) may be described as a period when results of epidemiologic long-term research are being applied in several fields.

Four specific areas receiving study include:

1. Further development of the risk factor concept with an attempt to delineate a ranking order for risk factors of the three major vascular provinces.

2. Testing clinical questions, e.g. the meaning and importance of hyperlipoproteinemia in the general population *outside* of laboratories, exclusively devoted to the study of fat metabolism, or the practical problems of drug intervention in hypertension and motivation for regular drug use.
3. Improvement of methods for screening of persons with risk factors—in particular screening methods for the general practitioner's office and concentration on those risk factors which could be influenced.
4. Research on methods in health education and intervention in the general public.

Within the framework of these new developments in prospective epidemiologic studies and research the Pooling Project has gained widest recognition. Data have been pooled from the Framingham Study, the Albany-, Tecumseh-, Los Angeles-, Minneapolis Studies as well as those from the Chicago Gas Company and Chicago Western Electric Company. A total of 7342 healthy males aged 30–59 years at the base line study were reexamined after a ten year observation period. Only 1249 men = 17% were free of three risk factors hypercholesterolemia, hypertension and cigarette smoking. The remainder had at least one risk factor (45%). Two risk factors were found in 30% and three risk factors in 8% of all men. The two last groups combined (i. e. 38% of 7342 men with 2 or 3 risk factors) contributed to the larger percentage (58%) of all new developing cases of ischemic heart disease within the decade from 1960 to 1970 and, among these, 62% of cases of sudden death (STAMLER and EPSTEIN, 1972).

In addition to the American Pooling Project, a number of epidemiologic long-term studies have been carried out during the past five years in the Scandinavian countries. These will be mentioned in some of the chapters. The new Center for Research in Myocardial Infarction which opened in 1973 at the Medical Clinic, University of Heidelberg, also actively participates in long-term epidemiologic research, initiated by WHO in several European countries.

Intervention studies with a multifactorial approach have to prove that the high incidence of ischemic heart disease may be lowered by modifying risk factors. Long-term studies, those from Framingham and Albany, N.Y., Honolulu, San Francisco, Puerto Rico and Evans County, Ga., have combined their efforts to test

the importance of hyperlipoproteinemia for the development of ischemic heart disease in the general population. The Evans County Study is part of a national multicenter program for hypertension intervention and follow-up. This program has been projected for a total of 5 years where 5000 hypertensive patients are undergoing intensive therapy. An equally large number of hypertensives will serve as controls and their progress will be monitored while they are remaining under the prevailing system of medical care with their local medical doctors. A number of studies have been initiated by the National Heart and Lung Institute in Bethesda testing the multifactorial approach of combined dietary therapy for hypercholesterolemia, antismoking clinics, hypertension control and weight reduction. Although results of these new intervention studies will not be known for several years, physicians should begin to practice applied epidemiology now. Modern epidemiological research has worked out a priority list:

Table 1 summarises the results of prospective long-term studies and shows the relative value of several risk factors for each of the three major vascular beds (GORDON et al., 1971).

It is obvious that the risk for a single individual cannot be generalized from those tables. A smoker of 2 packs a day who may display other risk factors at the same time is by far at a greater risk, simply because of his chain smoking habit; or a hypertensive who has only a mildly elevated cholesterol carries a greater risk for ische-

**Table 1: Ranking
order of risk factors.**

Ranking order of risk factors	
1. Ischemic heart disease:	1. Hypercholesterolemia 2. Cigarette smoking 3. Hypertension 4. Hyperglycemia/Diabetes mellitus 5. Hyperuricemia/Gout 6. (indirectly) Obesity
2. Stroke:	1. Hypertension 2. Diabetes mellitus 3. Obesity
3. Intermittent Claudication:	1. Cigarette smoking 2. Diabetes mellitus 3. Hypercholesterolemia/ Hypertriglyceridemia

Table 2: Risk factor screening program

Number of cigarettes <input type="text"/>	Non-Smoker <input type="text"/>		
Height (cm) <input type="text"/>	Weight (kg) <input type="text"/>	Normal weight: Ideal weight:	Height in cm minus 100 = Weight (kg) Height in cm minus 110 = Weight (kg)
Systolic blood pressure (mmHg) <input type="text"/>	Diastolic blood pressure (mmHg) <input type="text"/>	Normal: Borderline: Hypertension:	100–139 systolic and 60–89 diastolic 140–159 systolic and/or 90–94 diastolic 160 and more systolic or 95 and more diastolic
Blood glucose (mg%) <input type="text"/>		In persons \leq 50 years: Normal: In persons $>$ 50 years: Normal:	$<$ 109 mg % fasting $<$ 119 mg % non-fasting $<$ 119 mg % fasting $<$ 129 mg % non-fasting
Cholesterol (mg%) <input type="text"/>		Normal: Borderline: Pathologic:	\geq 220 mg % 221–259 mg % \geq 260 mg %
Triglyceride (mg%) fasting <input type="text"/>		Normal: Borderline: Pathologic:	$<$ 150 mg % 150–180 mg % \geq 181 mg %
Uric acid (mg%) <input type="text"/>		Males: Borderline: Pathologic: Females: Borderline: Pathologic:	$<$ 6 mg % 6.1–7.0 mg % $>$ 7.1 mg % $<$ 5.5 mg % 5.6–6.0 mg % $>$ 6.1 mg %
Urea N (mg%) <input type="text"/>		Normal: Borderline: Pathologic:	$<$ 27 mg % 28–30 mg % $>$ 31 mg %
Creatinine (mg%) <input type="text"/>		Normal: Borderline: Pathologic:	0.5–1.3 mg % 1.4–1.5 mg % 1.6 mg % and above
Urine examination:	1. Sugar _____ 2. Albumin _____ 3. Blood _____ 4. Ketone _____ 5. Urobilinogen _____ 6. Bilirubin _____		

mic heart disease – following the lipid filtration hypothesis – since cholesterol, even if only elevated to a slightly higher than normal concentration, is continuously “pushed” into the intima of the coronary artery. Therefore his chances of developing progressive atherogenesis in the coronary arteries is much higher than in a man with normal or low blood pressure levels. The risk factor-screening program which we have used in several villages in the Eastern part of Switzerland and among factory workers, can be administered within 5 minutes: height and weight are determined, blood pressure is taken in the sitting position, smoking habits are recorded and blood is being drawn for glucose, cholesterol, triglycerides and uric acid. In case of hypertension two additional kidney function tests are being performed (creatinine and urea N). The first morning urine is tested with a test strip. The values for each individual are typed into the empty boxes on the record (Table 2) on the left side. Each examinee is confronted with his own laboratory results and can decide to seek medical care after comparing his own values with the normal, borderline and pathologic values, printed at the right side of this table.

Hypercholesterolemia

According to the results of the Framingham Study, hypercholesterolemia is at the top of the ranking order of risk factors for the development of ischemic heart disease.

All studies which have been carried out in the post-Framingham era (after 1970) have more or less confirmed this finding quantitatively. However, a 5-year prospective study comparing males in Europe and males in the United States (KEYS et al., 1972a) has raised doubts whether an equally high cholesterol level might carry the same risk for the development of myocardial infarction on both sides of the Atlantic. The predictability for myocardial infarction, using the combination of age, cholesterol level, blood pressure value and smoking habits was roughly twice as high in American males as European men of the same age (similar blood pressures, serum cholesterol levels and smoking habits). However, among the European countries, nations were included which customarily have widely varying nutritional habits, cholesterol levels and different incidence rates of myocardial infarction – Finland, Italy, Greece, Holland and Yugoslavia. For many years Finland has shown the highest death rates from myocardial infarction in the world, whereas Italy, Greece and Yugoslavia rank much lower on the international list in this respect. A separate comparison between the Finnish and American data reveals an identical predictability of elevated cholesterol levels for a high risk of myocardial infarction.

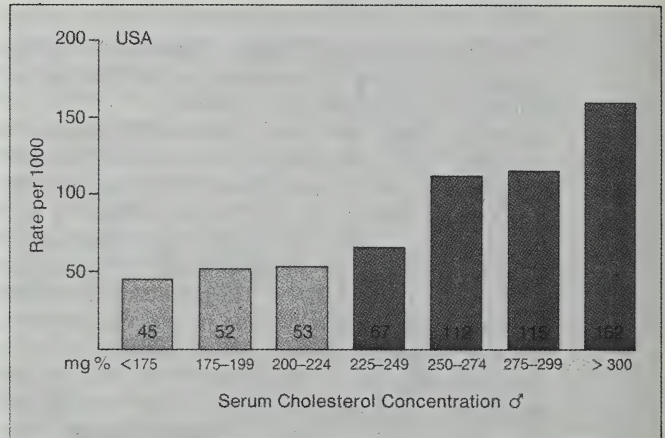
In addition, it is now possible to compare the 10 year incidence rate between two countries – USA and Norway. The Pooling Project (Fig. 1) comprises a 10 years observation period of 7342 American males between 30–59 years old when first examined. The serum cholesterol concentration, which was determined just once in 1960, was taken as the base line value and was used for the prediction of the incidence of ischemic heart disease within the subsequent ten years.

At a cholesterol level of 225 mg% there is a relatively low incidence rate of ischemic heart disease. At a cholesterol level of 225–249 mg% there is a definite increase and above 250 mg% the incidence is doubled in comparison to cholesterol levels below 225 mg% (STAMLER and EPSTEIN, 1972).

A parallel study (WESTLUND and NICOLAYSEN, 1972) was conducted in Oslo, also comprising a 10 years observation period (Fig. 2).

Fig. 1: Incidence of myocardial infarction per 1000 males aged 30-59 years within a 10 years observation period.

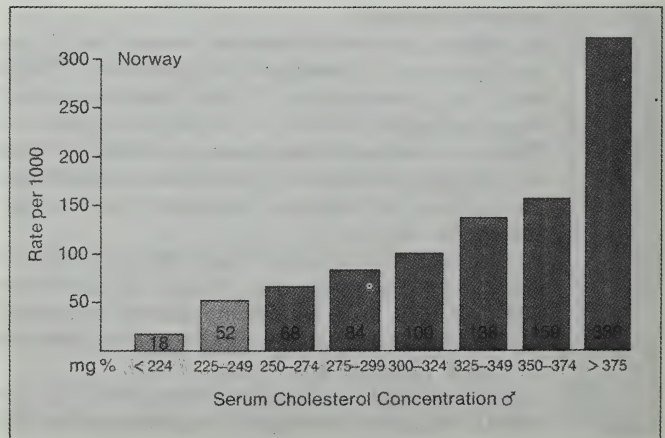
STAMLER and EPSTEIN, *Prev. Med. 1* (1972) 27.



Between 1958 and 1960 3676 men aged 40-49 years were examined. Again cholesterol was determined only once and this base line level was used as a predictor for the development of myocardial infarction, angina pectoris and sudden death within the subsequent ten years. The authors regard cholesterol as a unique predictor for myocardial infarction. "High cholesterol is about as dangerous as high blood pressure, but men with low cholesterol

Fig. 2: Incidence of myocardial infarction per 1000 males aged 40-49 years within a 10 years observation period.

WESTLUND and NICOLAYSEN, *Scand. J. Clin. Lab. Invest. 30* (1972) Suppl. 127.



have a lower mortality than men with low blood pressure . . . Serum cholesterol occupies a special position among the various predictors of myocardial infarction incidence. According to the risk curve, the Oslo incidence could be reduced to $\frac{1}{3}$ if the mean cholesterol in the male population at age 40 could be held at 220 mg % rather than at 270 mg %, other contributions to risk remaining equal" (WESTLUND and NICOLAYSEN, 1972).

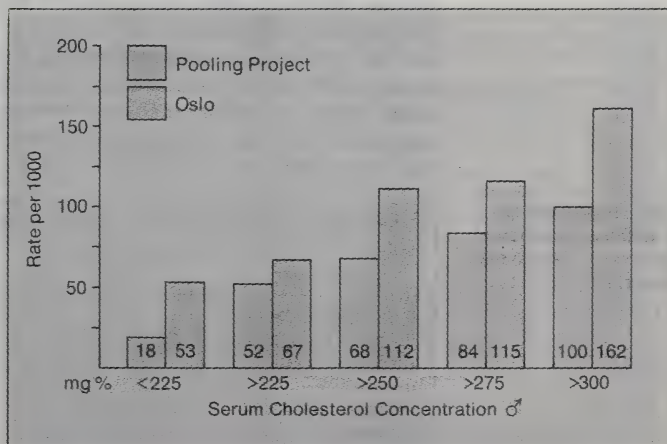
It is interesting to note that the incidence of ischemic heart disease in Norwegian males consistently lags behind the incidence of the American males at each cholesterol level (Fig. 3). Whereas among 1000 Americans aged 30–59 with a cholesterol level below 225 mg % 53 males developed ischemic heart disease, the same incidence rate is seen among Norwegian men at a cholesterol level between 225 and 249 mg %. Similarly, Americans with cholesterol levels between 225 and 249 mg % show an incidence rate of 67 per 1000, while Norwegians reach this incidence rate of 68 per 1000 at cholesterol levels between 250 and 274 mg %.

Dietary treatment is indicated for all males, on both sides of the Atlantic, as long as cholesterol levels are 250 mg % or higher. The ideal serum cholesterol concentration obviously is below 200 mg %. "Normal" cholesterol levels of 220 mg % are desirable for adults at all ages (FREDRICKSON, 1972).

A study by WELCH et al. (1970), correlating findings from cinecoronary angiography with cholesterol levels in young men under

Fig. 3: Comparison of the incidence of ischemic heart disease per 1000 males according to base line cholesterol concentrations in American and Norwegian males.

STAMLER and EPSTEIN, *Prev. Med.* 1 (1972) 27, and WESTLUND and NICOLAYSEN, *Scand. J. Clin. Invest.* 30 (1972) Suppl. 127.



Tab. 3: Correlations between serum cholesterol concentrations and pathological coronary angiograms.

WELCH et al., *Circulat.* 42 (1970) 647.

Cinecoronary angiography findings and serum cholesterol concentration in 657 men under the age of 40			
Serum cholesterol (mg %)	Number of patients	Significant findings Number	%
< 200	169	33	20
201-225	90	34	38
226-250	113	54	48
251-275	99	59	60
276-300	73	56	77
301-350	69	55	80
> 350	44	40	91

Table 4: Five rules for the normalization of elevated cholesterol levels.

age 40 (Table 3) agreed conclusively with epidemiologic data. The general population in Western countries has become accustomed to high average cholesterol levels. While it is desirable to change the nutrition of all people to lower these high average cholesterol levels, at the present time this appears to be wishful thinking. At this stage lipid determinations should be performed routinely ideally during adolescence. Adolescents who show serum cholesterol concentration of 200 mg % or higher should observe the dietary restrictions outlined in Table 4 (HEYDEN, 1974). Particular attention has to be paid to the so-called invisible, hidden fats (Table 5). Some of our patients use the argument that our parents and grand-parents have used much more fat than the present generation. A graphic review (Fig. 4) of the fat consumption between 1900 and 1970 demonstrates that the use of invisible fats in the 70ties has increased above 50 per cent of the total fat consumption (Fig. 5: Fat intake per person in Germany in 1972 reached 51 kg per year of which 26 kg were derived from invisible

Table 5: Invisible fats in different food items.
HEYDEN, S., *Dtsch. Med. Wschr.* 99 (1974) 141.

Edible Portion 100 g	Fat g	Cholesterol mg	Carbo-hydrates g	Sac-charose g
Chocolate cake with cream layers (baked)	15.6	100	41.7	26.9
Biscuit (baked)	4.2	167	72.0	36.0
Ice cream	12.0	40	19.6	14.3
Whipped cream	30.0	102	2.9	—
Chocolate	32.8	—	54.7	44.6

5 rules for the normalization of elevated cholesterol levels

1

Rule

Weight reduction (rule of the thumb):
Height in cm minus 100 = normal wt. in kg,
Ideal weight: height in cm minus 110 =
ideal weight in kg

2

Rule

Lowering of the total fat intake,
particularly of the invisible fat
(meat and meat products, milk and milk
products, baked goods)

3

Rule

Reduced cholesterol intake to less than
300 mg per day.

4

Rule

Relatively higher consumption of vegetable
fats and vegetable oils (margarine
and oil), safflower oil, sunflower-seed oil,
corn oil, soy bean oil – but excluding
olive oil, peanut oil or products made with
coconut fat or palmkern oil.

5

Rule

Avoidance of animal fat (pork fat, skin of
chicken and turkey), substitution of butter
by margarine, whole milk by skim milk,
fat cheese by low fat cheese, regular
yoghurt by skim milk yoghurt,
cream cheese by cottage cheese.

Average cholesterol content in various food items (milligram/100 g)

Meat:	
Pork (extra meager)	70
Beef	70
Veal	90
Mutton	65
Lamb	70
Venison	110
Inner Organs:	
Pork liver	360
Beef kidney	350
Calf liver	420
Thymus	290
Brain	3100
Chicken:	
75	
Fish:	
Caviar	300
Lobster	150
Oysters	150
Crab	150
Sole	50
Red perch	40
Mackerel	35
Cod fish	30
Milk + Milk products:	
Whole milk (3.5% fat)	10
Skim milk	3
Double cream cheese (60–70% fat)	105
Fat cheese (45%)	90
Fat cheese (40%)	75
Fat cheese (30%)	57
Low fat cheese (20%)	30
Low fat cheese (10%)	12
Ice cream	45
Fat:	
Butter	280
Pork fat and other animal fats	100
Vegetable margarine	0
Eggs:	
1 Egg	280
Egg white	0
Egg yolk fresh (100g)	1400

Fig. 4: Fat consumption between 1900 and 1970.*
Margarine Institute for Healthy Nutrition, Hamburg

* F.R.G.

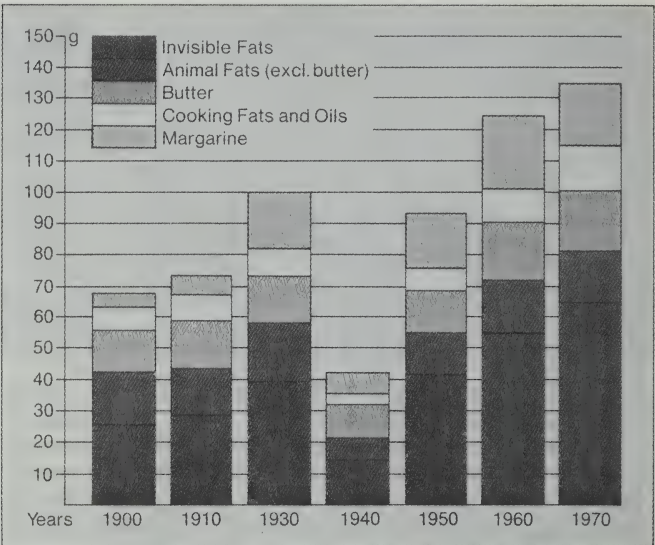


Fig. 5: Fat consumption 1972.*
Margarine Institute for Healthy Nutrition, Hamburg

* F.R.G.

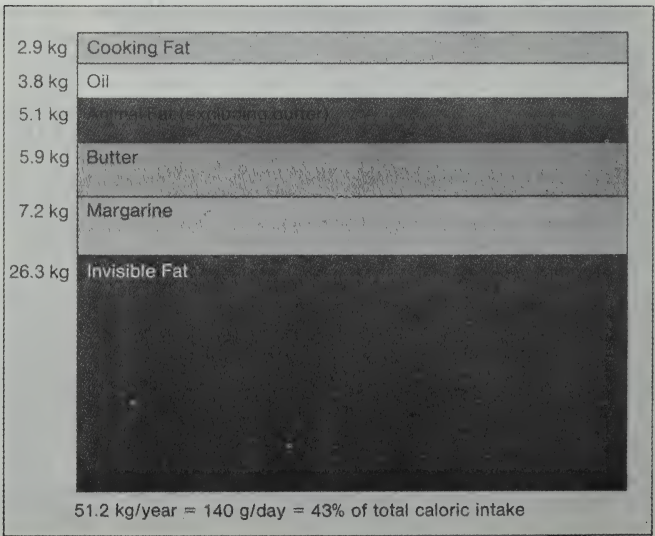
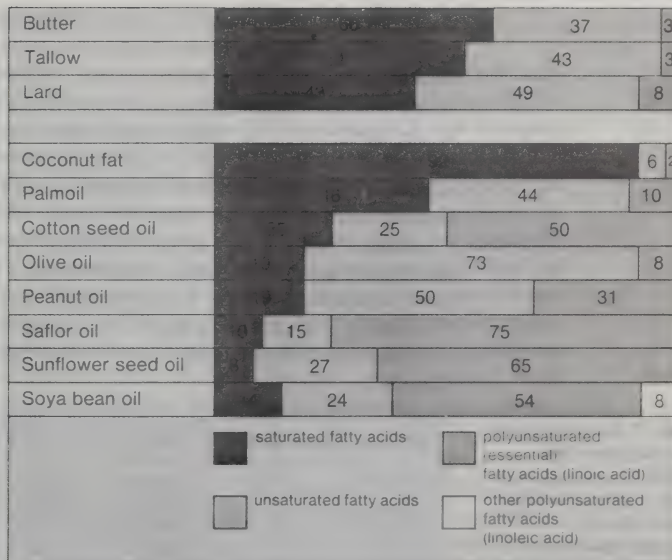


Fig. 6: Fatty acid content of different fats.
Margarine Institute for Healthy Nutrition, Hamburg.



fats). Table 5 presents typical examples of animal fat in baked goods, milk products and chocolate.

Of equal importance is the limitation of animal fats, the saturated fatty acids and the *relatively* higher consumption of polyunsaturated fatty acids (Fig. 6).

Serum cholesterol concentrations of women require special mention: Women have higher serum concentrations of alpha-lipoprotein-cholesterol than men. Table 6 illustrates typical relationships.

The alpha-cholesterol levels among women in East Finland as well as in West Finland are found to be 56–57 mg% while their husbands have levels between 39–41 mg%. Conversely, the beta-

Tab. 6: Average cholesterol levels in lipoprotein fractions in the serum of healthy Finish males, 40–49 years old, in comparison to their wives.
KEYS, A., J. Amer. Dietet. Ass. 51 (1967) 508.

Persons examined		Number	Cholesterol (mg%)		
			α	β	total
Males	East Finland	20	39	212	251
Females		20	56	182	238
Males	West Finland	28	41	198	239
Females		28	57	170	227

cholesterol levels in men are approx. 30 mg% higher than in women. "This fact is the main reason for the general believe that alpha-cholesterol, unlike beta-cholesterol, does not promote atherosclerosis; the alpha-fraction may even be protective, thus total cholesterol values do not have the same meaning for women as for men. According to theory about the effect of cholesterol on atherogenesis, a total cholesterol value of 230 in a man is at least as bad as a value of 245 in a woman" (KEYS, 1967).

"Normal" (see Fig. 1) cholesterol values lower than 220 mg% in males were associated with a relatively high incidence of ischemic heart disease in Evans County in the age group 35-44 years (59/1000) – an incidence rate which is found among women with identical cholesterol levels only in the age group 65-74 years (Table 7).

Tab. 7: Serum cholesterol concentrations 1960/62 and incidence (per 1000) of ischemic heart disease in a 7-years observation period in Evans County (1967/69).

TYROLER et al., Arch. Int. Med. 128 (1971) 907.

1960/62 Cholesterol	Age	≤ 219 mg%	≥ 220 mg%
1967/69 IHD in men	35-44	59	66
	45-54	65	96
	55-64	122	148
	65-74	179	323
1967/69 IHD in women	45-54	29	30
	55-64	39	42
	65-74	59	178

In women at the age of 45-54 years the incidence of ischemic heart disease *per 1000* is 29 and 30 at cholesterol levels *below 220 and above 220 mg%*, respectively – in other words, nonsignificant differences. In women aged 55-64 years the same picture emerges: Below 220 mg% the incidence is 39/1000 and above 220 mg% 42/1000! Only after age 65 is a three-fold increase of the incidence rate to 178/1000 found.

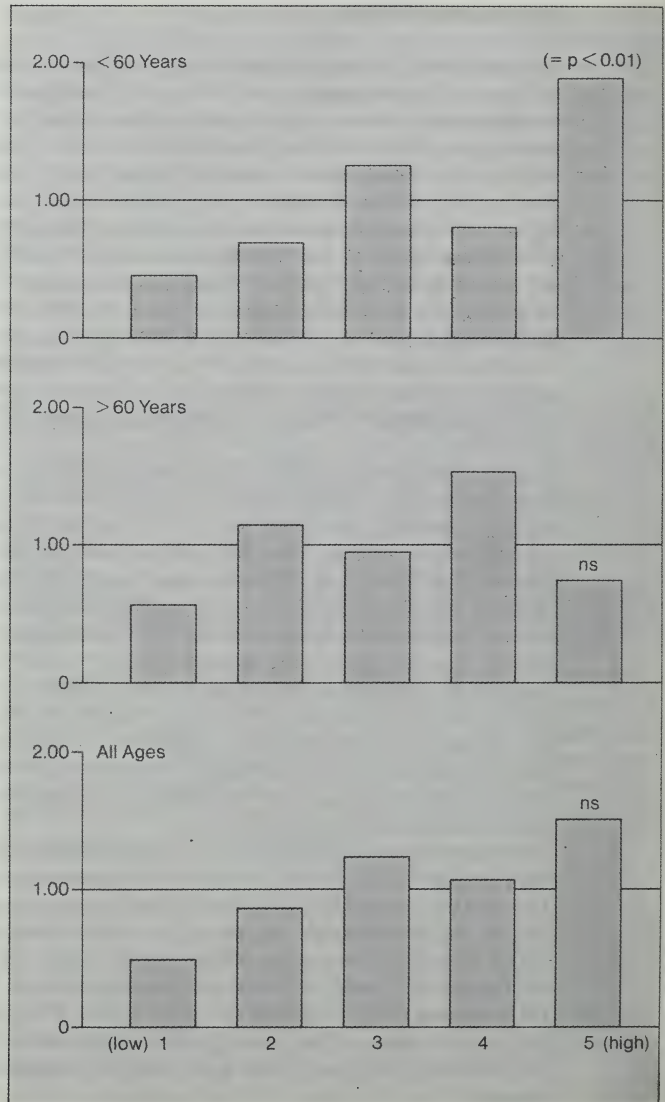
Hypertriglyceridemia

The past decade was one of intensive research into the importance of hypertriglyceridemia as a risk factor in its own rights for the development of ischemic heart disease. In the early 60ties it appeared that serum triglycerides (upper normal levels for fasting triglycerides: 150 mg %) might be of equal or even greater value in the predictability than cholesterol levels. These assumptions were based on indirect estimation methods of triglycerides. Two prospective studies (Albany and Framingham) demonstrated that the predictability of triglycerides is of less value than that of cholesterol (BROWN et al., 1965). Only "in women over 50, prebeta-lipoprotein was superior to cholesterol in discriminating potential coronary heart disease cases. Risk of coronary heart disease in men can be estimated using any of the lipids; however, none proved more useful than an accurate total serum cholesterol" (KANNEL et al., 1971).

CARLSON and BÖTTIGER (1972) and BÖTTIGER and CARLSON (1973) assessed the role of serum triglycerides in the Stockholm prospective study with 71 men developing I.H.D. within 9 years. Fig. 7 "shows the rate of new events for persons below age 60, over age 60 and for all ages. The subjects in each decade have been grouped into quintiles according to their triglyceride value, quintile 1 thus comprising the subjects with the 20 % lowest triglyceride values etc. The rate given is the incidence (number of new events divided by the number of individuals at risk) in each quintile, divided by the incidence rate of the whole population, i.e. the rate 1.00 (broken line) is that in the population. Statistical tests were performed to see whether the rate in the extreme quintile is different from the rate in the other 4 quintiles. Two astericks indicate a significance level of $p < 0.01$."

Obviously, for men beyond age 60 and for all ages combined, initial TG values are of no predictive value in ischemic heart disease. The men below age 60 show a trend of an increasing rate from the first to the third quintile. However, the rate of subjects in the fourth quintile is lower again, almost similar to the rate in the second quintile. There is no linear relationship between increasing TG levels and I.H.D. rates. Neither the 1972 nor 1973 publication indicate how many of the 71 men in this prospective study were in the below-age 60 group. How many men were actually in each quintile?

Fig. 7: Rate of new events of coronary heart disease in relation to initial plasma triglyceride levels and age.
BÖTTIGER and CARLSON,
Skandia Internat.
Symp. 9/19 (1972)
21, Nordiska
Bokhandels Förlag,
Stockholm (1973).



We do not know and agree with Stamler (1973) that "the published data do not necessarily warrant this inference. It is very possible that hyperprebetalipoproteinemia has significance for atherogenesis chiefly, perhaps solely, because of the associated hypercholesterolemia. No evidence is available indicating that – in the absence of hypercholesterolemia – hypertriglyceridemia (whether from endogenously synthesized VLDL molecules or from absorbed chylomicrons) is associated with intensified atherogenesis."

Practical experience with hyperlipoproteinemia type II B, III, and IV patients generally shows an amazing lability of the serum triglyceride level under dietetic changes, foremost among them weight loss as exemplified in a 40 year old woman after weight loss of 35 kg (Fig. 8).

In hyperlipoproteinemias LDL is one of the atherogenic factors. Low-density or beta-lipoproteins normally account for almost $\frac{3}{4}$ of cholesterol and are mainly derived from the VLDL (very low

Fig. 8: Influence of weight reduction on cholesterol and triglyceride levels in hyperlipoproteinemia type III. HEYDEN, S. in: *The Role of Fats in the Human Diet* (VERGOESEN, ed. Academic Press Inc., London 1975).

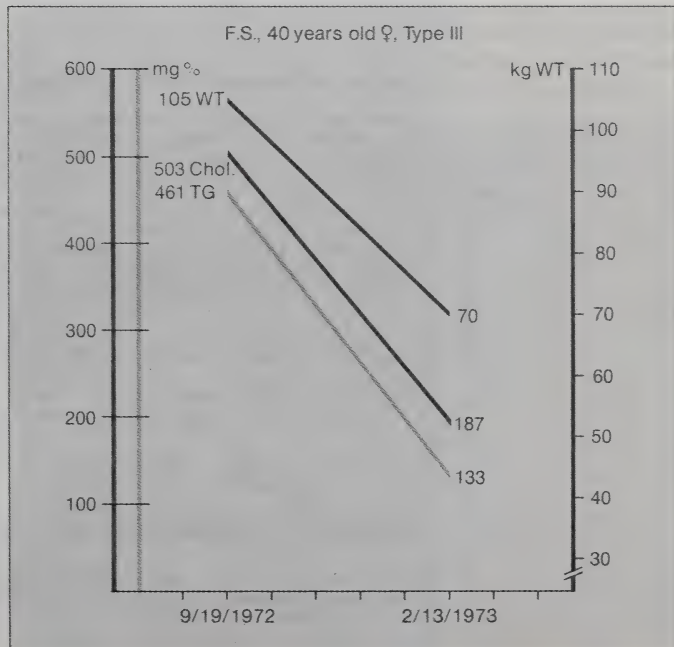
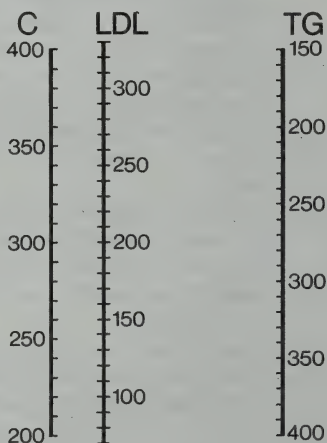


Fig. 9: Nomogram for separation of type II B and type IV.

With kind permission
of Dr. FREDRICKSON,
Mod. Conc. Cardiovasc.
Dis. 41 (1972) 31-36



Nomogram for separation of type IIB and type IV.

When serum cholesterol concentration is elevated and triglycerides are increased to a level between 150 and 400 mg/100 ml, the estimation of plasma LDL concentration helps to differentiate between type IIB and type IV (C = Cholesterol, TG = Triglycerides).

Lay a straight edge connecting the known plasma concentration of cholesterol on line C and the triglyceride concentration on line TG. Read the LDL concentration where the straight edge crosses line LDL (LDL: Low-Density- or Beta-Lipoproteins; LDL concentration in terms of mg per 100 ml of cholesterol in this lipoprotein).

Separation between type IIB and IV

As a rough rule, LDL above 180 means type IIB.

When LDL levels are lower, this constellation more likely represents type IV.

Example: Cholesterol = 320 mg/100 ml
Triglycerides = 250 mg/100 ml
LDL = 225 mg/100 ml

This is type IIB because triglycerides are abnormally high.

With kind permission of Dr. Fredrickson, Mod. Conc. Cardiovasc. Dis. 41: 31-36, 1972.

density or pre-beta-lipoprotein) metabolism. The LDL level is easily estimated from the nomogram provided by Dr. FREDRICKSON (Fig. 9).

In a 57 year old patient with type II A (Fig. 10) the LDL level was normalised by weight reduction alone.

In another man with type II A (aged 40) cholesterol and triglyceride levels decreased considerably. However, his LDL did not reach a normal level below 160 (Fig. 11).

We determined triglyceride levels in 1800 adults in Evans County, Georgia (Table 8). Age-adjusted mean levels of triglycerides in 114 patients with ischemic heart disease and 45 patients with cerebrovascular disease showed no significant differences in both sexes and both races when compared with healthy individuals (HEYDEN et al., 1972 a).

The obvious disadvantage of a prevalence study such as this is that triglyceride levels could be examined only in healthy persons and in the survivors of vascular diseases. Any association found between elevated serum triglyceride concentrations and manifestations of cardio- and cerebro-vascular disease would, therefore, be an underestimate since the victims of fatal myocardial infarction and stroke with possibly elevated values were not examined.

Fig. 10: To measure the effect of therapy, this nomogram may even be used in type II A by extending the triglyceride scale to 100.

HEYDEN, S., in: *The Role of Fats in the Human Diet* (VERGROESEN, ed. Academic Press Inc., London 1975).

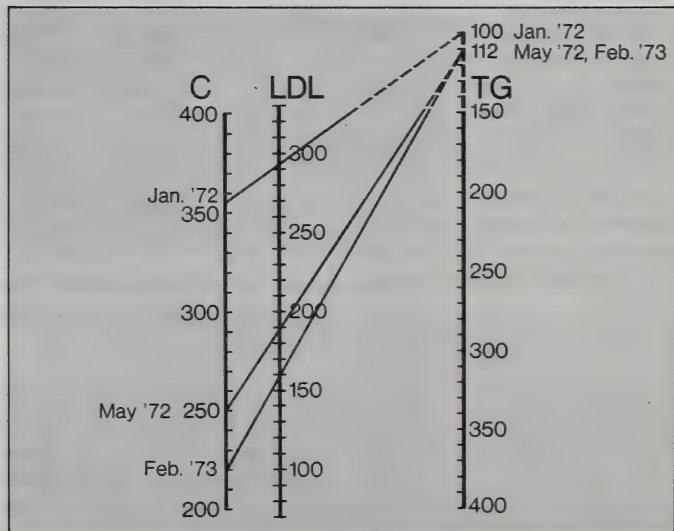
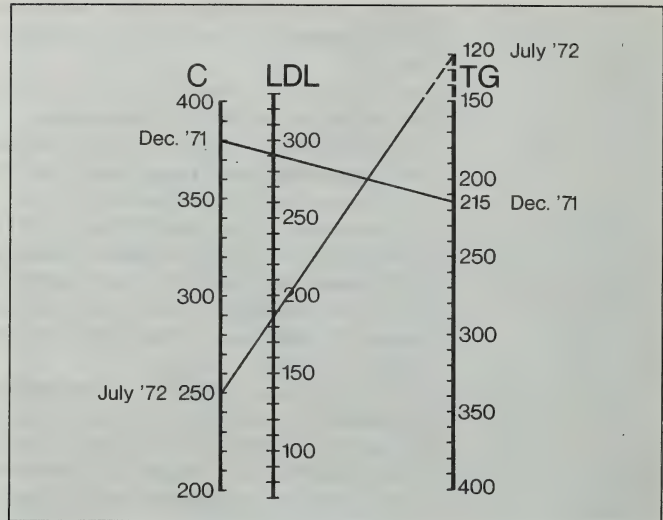


Fig. 11: To measure the effect of therapy, this nomogram may even be used in type II A by extending the triglyceride scale to 100.

HEYDEN, S. in: The Role of Fats in the Human Diet (VERGROESEN, ed. Academic Press Inc., London 1975).



Tab. 8: Age-adjusted triglyceride levels in persons with and without IHD and stroke.

HEYDEN et al., Ärztl. Praxis 93 (1972 a) 4571.*

* Number of subjects appear in parentheses.

	WM	WF	BM	BF
With IHD	133 mg% (59)	117 mg% (28)	77 mg% (8)	108 mg% (19)
Without IHD	127 mg% (506)	126 mg% (615)	95 mg% (222)	99 mg% (343)
With Stroke	128 mg% (26)	134 mg% (3)	95 mg% (9)	121 mg% (11)
Without Stroke	128 mg% (539)	125 mg% (635)	95 mg% (221)	99 mg% (351)

Differences in the triglyceride levels between subjects with and without cardiovascular disease were not statistically significant by covariance analysis.

The entire population was stratified according to the Quetelet Index, with group I constituting the lightest persons and group III the heaviest persons. Mean fasting triglyceride levels were lowest in group I, and highest in group III. Differences became less noticeable beyond age 50 in males and beyond age 60 in females (Table 9).

Tab. 9: Age-adjusted mean triglyceride levels in white males and white females.

HEYDEN et al., *Ärztl. Praxis* 93 (1972a) 4571.

Age 1967	White Males			White Females		
	Mean	S.D.	n	Mean	S.D.	n
25-34	132	121	64	104	111	69
1 *	88	48	23	89	45	37
3	186	198	19	165	210	16
35-44	129	92	70	118	76	77
1	103	48	18	109	81	38
3	154	128	28	153	91	16
45-54	136	98	143	130	110	168
1	96	36	43	104	59	54
3	133	55	49	161	160	53
55-64	128	60	156	127	92	160
1	117	65	43	114	71	35
3	142	63	58	140	114	80
65-74	108	46	73	131	64	115
1	100	45	33	128	64	28
3	117	41	21	145	66	44

* Quetelet-Index:
 1 = ≤ 3.30 (lean, normal weight) 3 = ≥ 3.80 (obese)

Among 195 white men, normal weight at age 20 and gaining more than 30 lbs., mean triglyceride levels were almost 20 mg% higher than in the more weight-stable group of 194 men. The *age-adjusted triglyceride levels were significantly different at the $p = .01$ level*. As expected the "ideal" group, normal weight at age 20, gaining very little, and the least ideal group, overweight at age 20, gaining the most, showed large differences (34 mg%) in triglyceride levels which were again statistically highly significant ($p < 0.005$) (Table 10).

Men classified in the professional occupations and office trades had higher mean triglyceride levels, whereas laborers and farm occupations had lower levels. A short-term triglyceride reduction

Tab. 10: White males, weight at age 20, weight gain and mean triglyceride levels.

HEYDEN et al., *Ärztl. Praxis* 93 (1972a) 4571.

		Weight at Age 20 White males	
		< 150 lbs.	> 150 lbs.
Weight gain	< 30 lbs.	a. (194 men) 114 mg%	b. (84 men) 123 mg%
Weight gain	> 30 lbs.	c. (195 men) 134 mg%	d. (82 men) 148 mg%

during endurance exercise among men has been observed by others and has raised hope that physical training may have a beneficial influence on the prevention of ischemic heart disease via lowering serum triglycerides (KÖNIG, 1973). However, if triglycerides play only a secondary role in the development of ischemic heart disease, this reduction may have no effect (Table 11).

Tab. 11: Occupation and triglyceride levels.
HEYDEN et al., *Ärztl. Praxis* 93 (1972 a) 4571.

	White males n	Mean (mg%)	S.D.
Professionals	154	148	(117)
Office Trades	169	124	(60)
Non-Farm Laborers	63	113	(58)
Farm Owners	112	118	(72)
Farm Laborers	48	117	(52)

On the other hand it was pointed out that coffee drinking may elevate triglyceride levels. We were unable to demonstrate any differences among heavy coffee consumers and non-coffee drinkers in the Evans County study. Slight increases of the serum triglyceride concentration after caffeine ingestion are without any clinical importance (HEYDEN et al., 1972 b).

The mean triglyceride levels among diabetics as a group are slightly higher than among non-diabetics (Table 12).

Tab. 12: Co-variance analysis of triglyceride levels in diabetics and non-diabetics by race and sex, using age as the co-variate.
HEYDEN et al., *Ärztl. Praxis* 93 (1972 a) 4571.

	WM	WF*	BM	BF
Non-diabetic	127 mg% (503)	122 mg% (572)	94 mg% (209)	93 mg% (312)
Diabetic	139 mg% (43)	175 mg% (42)	106 mg% (15)	113 mg% (39)

*p = .01, the only significant difference found between diabetics and non-diabetics in all four race/sex groups.

Conclusion

We agree with STAMLER (1973), "on the basis of currently available data, serum cholesterol is the best single measurement for assessing risk of premature atherosclerotic disease. Fasting serum triglycerides or lipoprotein (e. g. as determined qualitatively by paper electrophoresis) are not superior predictors of risk". A preliminary

analysis of the results of paper electrophoresis between 106 patients aged 45 years and older with ischemic heart disease and 645 healthy, non-selected "probability persons" above age 45 from the Evans County Study can be summarised as follows: 18% of patients with IHD had hyperlipoproteinemias – but so did 19% of persons without ischemic heart disease! It seems particularly important to mention that while 79% of the patients with ischemic heart disease had no typed hyperlipoproteinemia, 72% of the healthy persons did not show any type of hyperlipoproteinemia. Type II was found in 6% of patients with myocardial infarction and among 7% of healthy persons, type IV among 10% of patients with myocardial infarction and in 11% of the healthy persons. We conclude that the predictability of the lipoprotein electrophoresis for the development of ischemic heart disease disappears after age 45. On the other hand, when cholesterol levels are taken separately in our prospective study, the incidence of ischemic heart disease was twice as high in those with a serum cholesterol concentration of 260 mg% (1960–62) as in those with cholesterol levels below 220 mg%, when measured seven years later. This statement includes all age groups up to the 6th decade! (TYROLER et al., 1971).

Cigarette Smoking

Cigarette smoking is an independent risk factor for the development of three manifestations of ischemic heart disease including myocardial infarction and sudden death. The risk to develop myocardial infarction within 10 years is evident in Fig. 12: The Pooling Project which was a 10 year observation of 6427 men aged 30–59 years, divided into non-smokers, pipe-, cigar- and cigarette smokers, provides quantitative proof of the risk of developing myocardial infarction. The study placed ex-smokers in a similarly low risk category as non-smokers. One pack-a-day-smokers are twice as likely to develop ischemic heart disease as non-smokers. The incidence rate of chain smokers, on the other hand, is twice as high as that of smokers of 10 cigarettes or less per day.

Incidence of sudden death was found five times as high in chain smokers as in non-smokers in Framingham (Fig. 13). The Norwegian data (WESTLUND and NICOLAYSEN 1972) have confirmed that non-smokers have a lower incidence of myocardial infarction than smokers – “similar to men with normotensive blood pressures”.

The following facts derived from epidemiological research are important for the physician who daily confronts cigarette smokers.

1. HAMMOND's (1966) prospective study of 1 million men and

Fig. 12: Incidence of ischemic heart disease per 1000 men aged 30–59 years within 10 years observation.
STAMLER and EPSTEIN,
Prev. Med. 1 (1972) 27.

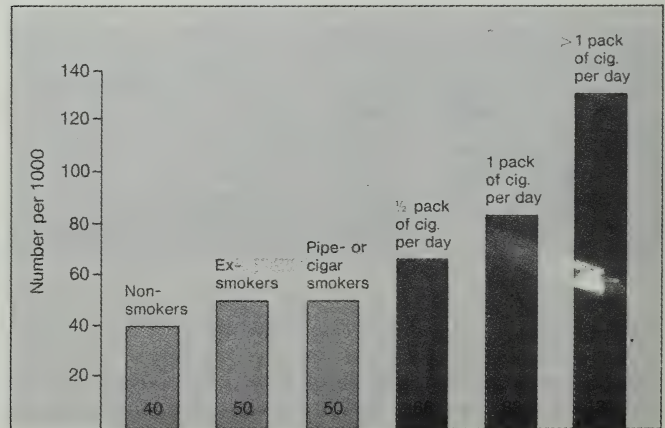
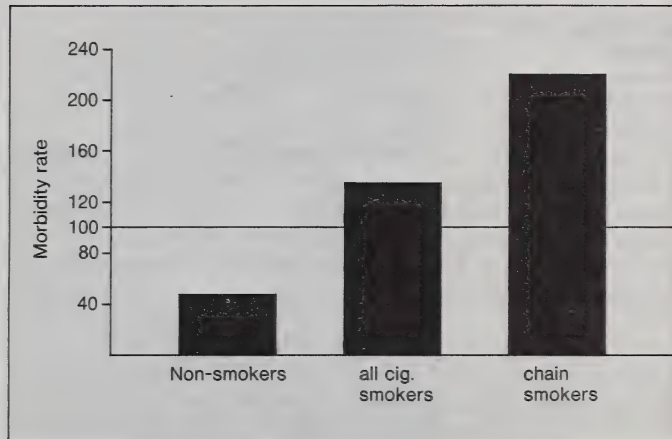


Fig. 13: Smoking and sudden death in the Framingham Study.

KANNEL, W. B., Hosp. Practice 85 (1970).



women in the United States was the first to demonstrate the remarkably low risk of coronary mortality for pipe- and cigar-smokers, i. e. less than 4 pipes per day and less than 2 cigars per day. The risk in this particular group is as low as that of non-smokers (see Pooling Project, Fig. 12).

2. Cigarette smokers who inhale only superficially have a lower risk for the development of ischemic heart disease than smokers who inhale deeply. Pipe- and cigar smokers who inhale have the same high risk as cigarette smokers.

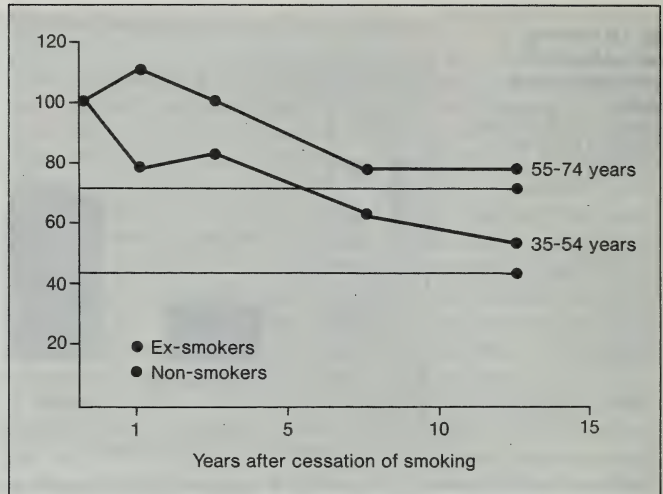
3. Ex-smokers – within 10 years – return to the low incidence prevailing in non-smokers. Older men (55–74 yrs. at the time of giving up smoking) initially show a higher mortality rate from coronary heart disease since the cessation of smoking in most cases was forced upon by symptoms of the patient (e.g. cardiovascular diseases, angina pectoris etc.). Mortality from myocardial infarction shows a continuing decreasing trend for the younger age group (Fig. 14, from HAMMOND, quoted by REID 1972).

4. Non- and ex-smokers have a better chance to *survive* a myocardial infarction than chain smokers. In the Pooling Project sudden death was recorded in 8 per 1000 ex-smokers, in 15 per 1000 pipe smokers and in 37 per 1000 chain smokers.

5. Anthropologists and psychologists still debate possible differences in constitution and personality structure of smokers and non-smokers. Meanwhile it has become general knowledge that

Fig. 14: Risk of coronary mortality among ex-smokers.

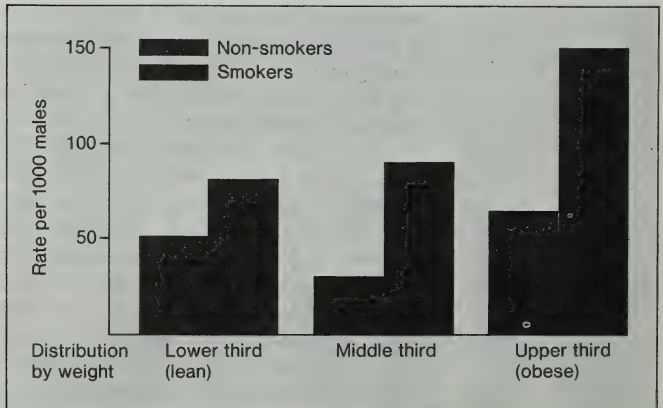
HAMMOND, C., Nat. Cancer Inst. Monograph 19 (1966) 127.



smokers are usually slim and have a lower blood pressure than the non-smoking counterpart, but these two observations obviously do not protect the smoker from myocardial infarction. In my opinion cause and effect get obscured if one accepts the ROSENMAN-FRIEDMAN theory. This hypothesis maintains that the aggressive type "A" is prone to myocardial infarction on the basis of his per-

Fig. 15: Age-adjusted incidence rates of IHD by body weight and cigarette smoking (white males).

HEYDEN et al., Arch. Int. Med. 128 (1971a) 915.



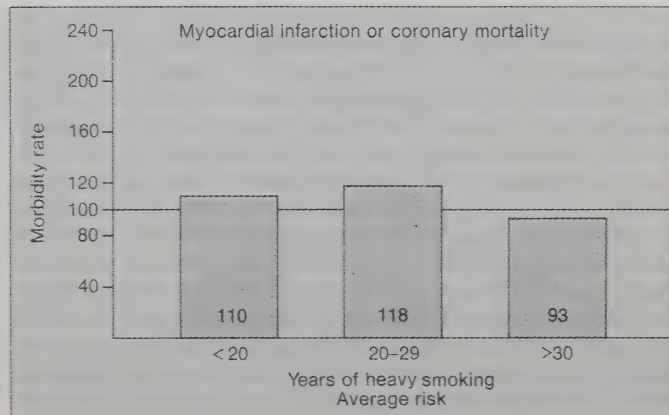
sonality structure and at the same time is predisposed to smoking, therefore making the association between heavy smoking and myocardial infarction secondary.

In the Chicago Electric Company Survey 1572 male subjects (40–56 years old) were questioned with the MMPI. “The results do not support the hypothesis that there is a definite personality pattern associated with smoking. Moreover a factor analysis of the basic data, too, fails to confirm the existence of a smoking personality. Personality theorists and those who seek to modify smoking habits may find it helpful to focus upon the stimulus conditions, external and internal, that are associated with smoking” (LEBOVITS et al., 1972).

6. The fear of gaining weight is the most frequent response of patients requested to give up smoking. The 7 year-incidence study of white males in Evans County demonstrates the relatively low risk of obesity in contrast to cigarette smoking (Fig. 15).

Non-smokers showed insignificant differences in the incidence rates of myocardial infarction regardless of whether they were normal-weight, slightly overweight or heavily overweight. On the other hand, cigarette smokers with normal weight, slight overweight and heavy overweight showed markedly increasing incidence rates (from 80 over 90 to 150/1000 males). The fattest cigarette smoker triples his risk for the development of myocardial infarction in comparison to the slim non-smoker (HEYDEN et al., 1971 a).

Fig. 16: Smoking and ischemic heart disease in the Framingham Study.
KANDEL, W. B., Hosp Practice 85 (1970).



7. Patients typically will use the argument of how many years they have been smoking ("I have been smoking for more than 20 years-it doesn't make sense to quit"). The number of years obviously does not play any role in the development of ischemic heart disease according to the Framingham Study. The number of cigarettes smoked daily, not the duration of habit, was found to raise the risk of ischemic heart disease (Fig. 16). There is little variation in risk of myocardial infarction or coronary mortality with duration of the smoking habit.

8. In an interesting study "Smoking and Morphometric Vascular Findings" by NÜSSEL and HÖPKER (1973), smoking was shown to be an independent risk factor. This is a very important finding since there were quite a few speculations that smoking may cause hypercholesterolemia or hypertriglyceridemia or that smoking may aggravate hypertension. Smokers and non-smokers do not differ in relation to other risk factors with the exception of a generally lower average blood pressure level in cigarette smokers! A strong correlation was found between smoking and pathologic changes in the femoral artery. No similarly high correlation with cigarette smoking was found in any other vascular bed.

This is further evidence for the ranking order of risk factors for the three main vascular beds shown in Table 1.

Hypertension

Definition of normal blood pressure: ≤ 139 mmHg systolic and ≤ 89 mmHg diastolic.

Borderline hypertension: 140–159 mmHg systolic and/or 90–94 mmHg diastolic.

Hypertension: ≥ 160 mmHg systolic and/or ≥ 95 mmHg diastolic.

In the past few years a number of blood pressure screening programs have been initiated in the United States among school children. Prevalence studies in the U. S. indicate that after age 15 five per cent of adolescents show blood pressures in the hypertensive range and after age 20 this percentage increases to 10%.

Several studies have shown that among the general adult population, essential hypertension predominates with 80 percent of all patients with the disease, though special hypertension clinics usually draw a larger percentage of patients with secondary hypertension.

For some years, the observation of an increased cardiac output in juvenile hypertensives has shed new light on the role of the heart in the etiology of hypertension: The heart, which long had been considered only a target in essential hypertension, has assumed a potential role as participant in its development. Early labile hypertension may have a high cardiac output and changes in peripheral resistance can be the consequence of continued high cardiac output.

SHAPIRO (1973) stated, it is "unrealistic to continue a search for a single and unique cause in essential hypertension; we have instead a plethora of causes . . . Processes which normally maintain blood pressure at levels adequate to perfuse blood and deliver oxygen throughout the body have in some way gone awry, and the checks and balances which are necessary to keep blood pressure from rising have become deficient. We know the mechanisms involved; we do not have sufficient data about how they interrelate and how they fail . . . Eventual further understanding of essential hypertension must derive from knowledge of the integration of the systems of blood pressure control. These include the renin-angiotensin mechanism, the sodium metabolism enigma, the psychogenic factors, the adrenal medullary and cortical phenomena, and the sympathetic nervous system reactivity. The clinician has operated on the basis of the hypothesis that hypertension is a multi-

factorial ailment. One has the impression, however, that he does it apologetically and considers that the treatments he uses are poor substitutes with which he is biding time until he knows the single, unique or specific cause of hypertension . . . We would submit now that fruition is unlikely. We will need to continue multifactorial therapy for a multifactorial disease."

On the basis of the presently available long-term studies, eight hypotheses about hypertension require reevaluation:

1. The wide-spread opinion that blood pressure increases with age ("Age plus 100 = systolic blood pressure") has not been upheld.
2. In contrast to the frequent statement "the height of the diastolic blood pressure is decisive", prospective studies have shown systolic blood pressure elevation to be of equal predictive importance.
3. The formerly held conviction that a significant artifact in blood pressure measurement occurs in subjects with fat arms is incorrect. Use of a long and wide (17 cm) cuff, will give true blood pressure readings in persons with obese arms.
4. Epidemiological long-term observations have given ample evidence that casual blood pressure readings, i. e. measurements obtained when the subject walks into the office, are of great predictive value for the subsequent course of the blood pressure development of an individual.
5. The thesis that adolescents always have a labile type of hypertension is wrong.
6. Sodium restriction to 1-3 g per day may be followed by properly instructed hypertensives to the same degree as drugs are taken, i. e. in approx. 50% of all hypertensives under a strict medical regimen.
7. Mild hypertension requires treatment - consisting at least of sodium restriction, regular observation and self-measuring devices at home. In women, oral contraceptives are contraindicated.
8. Caffeine neither causes blood pressure elevation nor aggravates preexisting hypertension.

Ad 1: Blood pressure not necessarily rises with age. In the "1000 aviator study" (HARLAN et al., 1962), individuals who had maintained their original weight within 5 lbs. between 1940 and 1958, showed only a systolic blood pressure increase of 1.4 mmHg, and diastolic blood pressure of 3.4 mmHg; however, among individuals with a gain in weight greater than 5 lbs. the mean systolic blood pressure increased 2.7 mmHg and the diastolic blood pressure 7.0

mmHg. In the Framingham Study, in men and women followed for more than 12 years, the risk of *developing* hypertension was 8 times greater in those 20% overweight than those who were 10% underweight at the time of the initial examination (KANDEL et al., 1967 a).

MIALL et al. (1968) in a longitudinal study of 2051 persons suggested that ageing plays no direct part in determining blood pressure levels. The 10-year follow-up with increases in blood pressures was correlated with changes in weight. The correlation co-efficient was positive in subjects under the age of 50 years. "Body build and weight factors play a role in determining pressure in young adults but do not appear important in causing subsequent increases in pressure. Thus, the analysis does not conflict with the hypothesis that weight may act as one trigger mechanism by causing pressures to rise to a level at which their subsequent rise is self-perpetuating." In our Evans County Study a statistically significant relationship between *weight gain* and both systolic and diastolic blood pressure was found, while the relationship between weight at age 20 and blood pressure levels was not significant (Table 13) in 7 years of observation.

Tab. 13: Correlation co-efficients of weight and blood pressure.

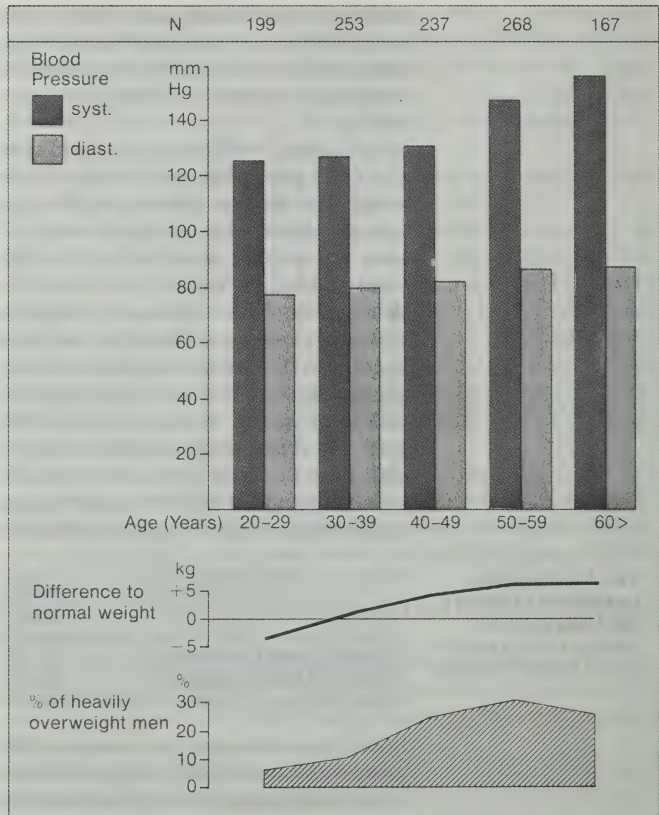
HEYDEN et al., Arch. Int. Med. 128 (1971b) 956.

	Weight gain	Weight at age 20
Systolic blood pressure	0.118	0.011
Diastolic blood pressure	0.285	0.028

Populations who show the least rise of blood pressure with age are those with lower average weight (CHIANG et al., 1969). The Geigy tables demonstrate the well-known increases in average weights from one 10-year age group to the next within the Western hemisphere. At least part of the increase of blood pressure with age can be explained by the average weight gain (see also Fig. 17).

Significant increases of mean blood pressure levels from the second to the sixth decade paralleled significant weight gains in our prevalence study in Swiss men. This group of 1124 healthy working Swiss males underwent marked weight changes, starting with an ideal average weight below age 30, and going into overweight levels (expressed in the deviation from the normal weight). The percentage of obese men increased particularly in the 30–40 year age group.

Fig. 17: Blood Pressure, Difference to Normal Weight, Percentage of Heavily Overweight Men (n = 1124).
 ESCHER et al. Schweiz. med. Wschr. 104 (1974) 1423.



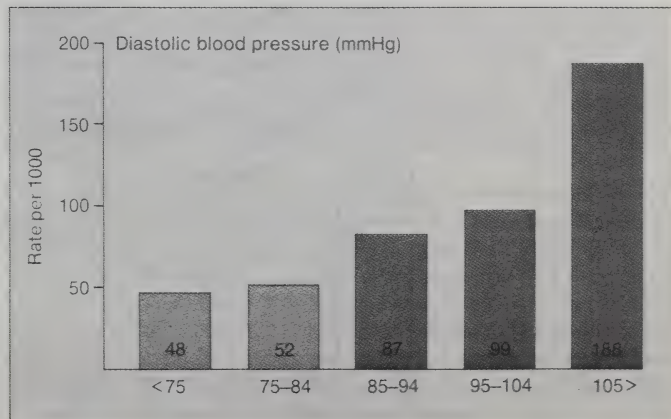
Ad 2: Systolic hypertension is as good a predictor for both cerebrovascular disease and ischemic heart disease, as diastolic hypertension. In most hypertensives, the systolic and diastolic blood pressure is highly correlated.

In addition, the study of the evolution of congestive heart failure (CHF) in the general population in Framingham revealed the risk of hypertensive patients to be six times that of normotensive persons: "Hypertension not only was a potent contributor to CHF incidence but was also the most common factor in the background of victims of CHF as it occurred in the population. Fully 75% of

those who acquired CHF during the 16 years period had prior hypertension." Again, it was noted: "An examination of the risk of CHF in the population classified at each biennial examination according to their systolic versus their diastolic pressures reveals little to suggest a stronger relation to the diastolic component . . . CHF was a lethal phenomenon with only 50% surviving for 5 years . . . Hypertensive heart disease with electrocardiographic manifestation of left ventricular hypertrophy is an ominous harbinger of CHF" (KANNEL et al., 1972).

Ad 3: The old question of whether the relationship between obesity and elevated blood pressure might be an artifact, due to the increased girth of the arm about which the blood pressure cuff is wrapped, has been answered in numerous articles. Recent studies, comparing direct intra-arterial recording of blood pressures with those measured indirectly by the auscultatory method, have shown no consistent difference between the two readings. KANNEL et al. (1967a), in the Framingham Study, compared upper arm and forearm pressures in the same persons and found similar readings whether or not their arm girth were large. Others found body weight to be correlated not only with blood pressure, but also with hypertensive heart disease, as demonstrated by electrocardiographic or X-ray evidence of cardiomegaly. In extremely obese patients, of course, a longer blood pressure cuff has to be used.

Fig. 18: Incidence of ischemic heart disease per 1000 men aged 40-59 years within a 10 years observation period.
STAMLER and EPSTEIN,
Prev. Med. 1 (1972) 27.

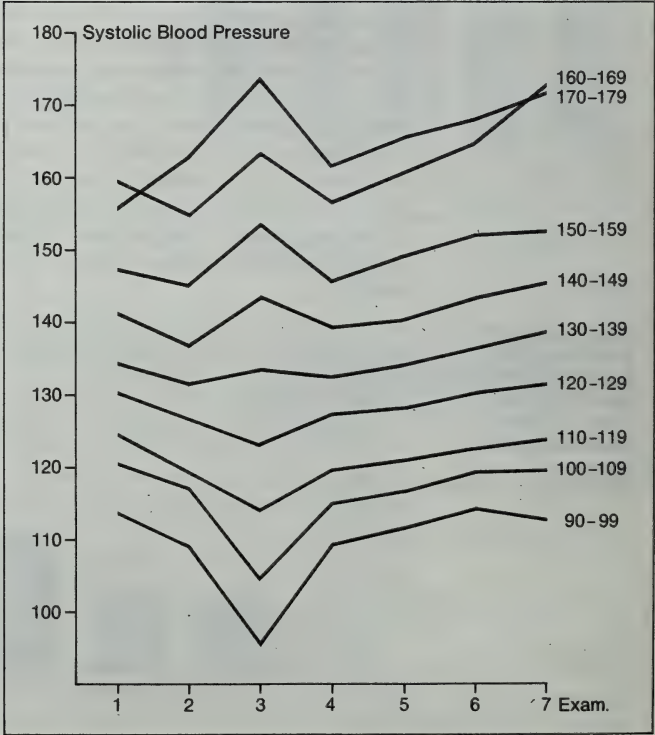


Ad 4: In all prospective epidemiologic long-term studies the so-called casual blood pressure measurement has been proven a very good indicator of subsequent blood pressure development and a predictor of the risk of stroke and ischemic heart disease. The Pooling Project is only one more example in this chain of evidence (Fig. 18).

The result of biennial blood pressure measurements within a 14 years observation period in the Framingham Study revealed a regression to the mean phenomenon: Men with higher blood pressures during exam 3 decreased in exam 4 and men low in exam 3 increased in exam 4 (Fig. 19).

More importantly, exam 4 through 7 showed interesting developments in relation to the baseline blood pressure level at exam 1.

Fig. 19: Mean Systolic Blood Pressure by Exam for Men Taking all 7 Exams and Classified According to Blood Pressure at Exam 3. Those Taking Hypotensive Drugs are Excluded.
The Framingham Study, FEINLEIB et al. (1969).



Men with systolic blood pressure levels below 130 mmHg remained at these levels whereas men with systolic blood pressure levels above 140 mmHg during the base line examination tended to increase their blood pressure levels further. In any examination of a large population one may find different blood pressures at the second and third measurements in comparison to the first examination. However, after a period of several years most examinees will return to their base line levels (if they were initially on the low side) or may increase with each subsequent examination (if the base line level was in the borderline or hypertensive range).

Ad 5: In the Evans County Study of 30 adolescents with hypertension (blood pressure > 140 mmHg systolic and > 90 mmHg diastolic), $\frac{1}{3}$ developed sustained hypertension after an 8 years observation period. Another third became normotensive and the remainder deserves the attribute "labile hypertension". Among the 11 adolescents with sustained hypertension, two deaths from cerebral hemorrhage occurred (Table 14).

Table 14: Clinical evaluation of 30 adolescents with elevated blood pressures and 30 normotensive controls in 1961 and 1968 in the Evans County Study, Ga.

HEYDEN et al., JAMA 209 (1969) 1683.

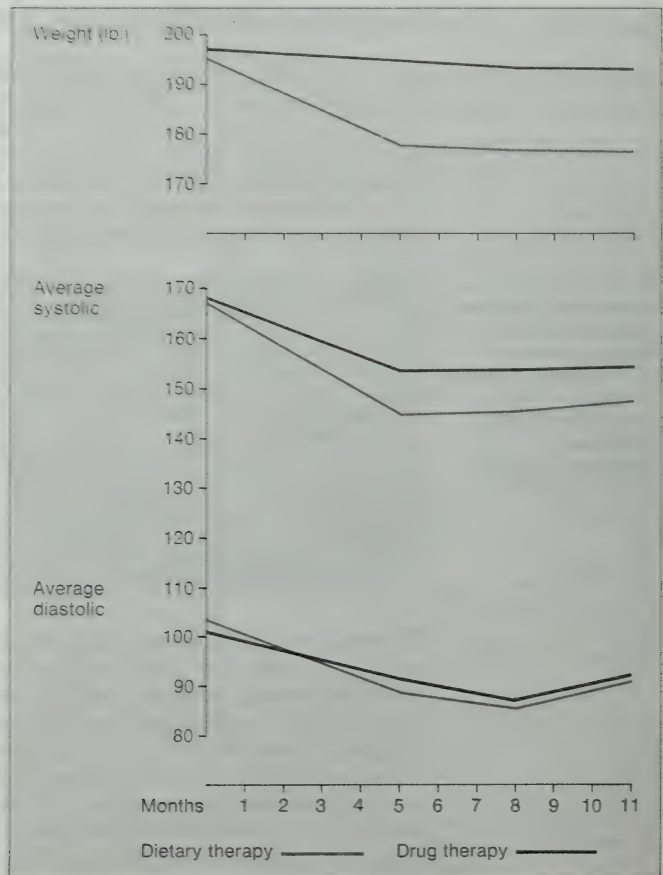
	1961	1968			Blood Pressure	
		Unchanged	Sustained Hypertension Asymptomatic	Sustained Hypertension with Vascular Complications	L	E
30 adolescents elevated blood pressures	7	5	6	12	...	
30 adolescents normal blood pressures	26	0	0	...		4

* L indicates lowered; E elevated

Follow-up was made of 116 male and female students aged 18–20 years, in a Swiss school, 3–4 years after the diagnosis of an elevated blood pressure. This pilot study revealed the following distribution: Of 75 youngsters with *borderline pressures* 3–4 years ago, 53 % had become normotensive, 43 % remained in the borderline group and 4 % showed sustained hypertension. Of 41 adolescents with hypertension 3–4 years ago, 41.5 % became normotensive and again 41.5 % were found borderline hypertensive, but 17 % remained in the sustained hypertensive group!

Ad 6: A 1-year intervention study in Evans County demonstrated that subjects in a free-living community who are both overweight and have elevated blood pressure, but are otherwise healthy, can be recruited into a weight reduction program. Of 63 subjects so randomized into the dietary program 58 remained in that program for one year and 62 of 64 in the control group were followed for the same period of time and frequently urged to see their physicians for medical treatment (HEYDEN et al., 1973 a). Parallel de-

Fig. 20: Effects of dietary therapy (group I) and drug therapy (group II) on weight and blood pressure in obese hypertensives.
HEYDEN et al. Clin. Sci. Mol. Med. 45 (1973 a) 209s.



creases in blood pressure occurred in these two groups but the dietary managed group (weight reduction and salt restriction to less than 3 g per day) had a decline of 18 mmHg systolic pressure and an average diastolic decrease of 13 mmHg. The "drug treatment" group had a decline of 12 mm Hg systolic blood pressure and an average diastolic decrease of 8 mmHg (Fig. 20).

One may seriously doubt whether hypertensive patients are taking their prescribed drugs regularly over an extended period of time. Pill-counts by nurses visiting patients at home revealed that maximally 50% of patients who had received prescriptions were taking their drugs regularly. Under these circumstances the salt restricted diet should be given a new chance – at least in those patients who are interested in dietary changes. The goal of dietary control of hypertension is lowering of the usual sodium intake of 15 g per day to 1.5 g per day – however, in many cases restriction to 3 g per day is sufficient.

Ad 7: Untreated hypertension, even mild, burdens individuals with an unreasonable risk to health and life. Table 15 and 16 present the results of two carefully monitored studies with placebo-"therapy" of mild hypertension over a period of 2.5 and 4 years in the first study and 3.3 years in the second study.

During the first 2½ years under placebo-"treatment", 39 subjects

Table 15: Two Follow-up Reports on Morbid Events in 196 Hypertensive Patients (Mean Blood Pressure 149/99 mmHg) under Placebo-"Therapy".
(Lit. Ref. see p. 44.)

Morbid Events	after 2½ years	after 4 years
Acceleration (DBP > 130 mmHg)	9	14
Cerebral hemorrhage	2	3
Myocardial infarcts	6	(6) *
Coronary insufficiency	3	7
Coronary deaths	2	(2) *
Cardiac enlargement	5	7
Retinopathy	3	4
LVH strain	12	14
Minor Events:		
LVH without strain	0	33
LAD	0	13
Arrhythmia	1	2
Conduction defect	1	(1) *
* Numbers in parantheses indicate the absence of new development of morbid events in these 3 categories.		

(20% of the patients) – average age 46 years – sustained 42 clinical events (left column of Table 15).

The right column of Tab. 15 demonstrates events during the total 4 years observation period: 76 subjects (39% of the patients) – average age 44 years – sustained 106 specific morbid events or complications.

Literature (Table 15):

1. U.S. Publ. Hlth. Serv. Hospit. Cooperative Study Group: Morbidity and Mortality in Mild Essential Hypertension. *Circulat.* 30 and 31 (1972) 110.
2. SMITH, W. McFATE: Benefits of Treatment. Paper presented at the Georgia Heart Association's 1973 Scientific Sessions for Physicians and Professional Nurses. Sept. 20–22 (1973) Atlanta, Ga.

Table 16: 380 Hypertensive Patients Randomised in 2 Groups. Average Observation Period 3.3 years, Mean Age: 51 Years.

FREIS, E. D., *Amer. J. Med.* 52 (1972) 664.

Baseline BP	Therapy	Placebo
Hospitalised	154/100 mmHg	158/101 mmHg
Ambulatory	162/104	165/105
Stroke	5	20
Congestive heart failure	0	11
Acceleration (DBP > 125 mmHg)	0	20
Ischemic heart disease	11	13
Other complications	8	6
Cardiovascular deaths	8	19
Summary of major complications	22	56

Table 17: Blood Pressure Levels Among Swiss Males 1973.

ESCHER et al., *Schweiz. med. Wschr.* 104 (1974) 1423.

Prevalence of Hypertension	n	%	Previously or Presently under Medical Care
n = 1114 Swiss Men, aged 20–65			
Manifest Hypertension			
Systolic \geq 160 mmHg and/or Diastolic \geq 95 mmHg	182	16	49 = 27%
Borderline Hypertension			
Systolic 140–159 mmHg and/or Diastolic 90–94 mmHg	272	24	27 = 10%
Normotension \leq 139/ \leq 89 mmHg	660	59	13 = 2%

We recently completed screening 1114 healthy employees and workers in a Swiss factory. Not surprisingly, the percentage of patients knowing of their mild or sustained hypertension and/or undergoing medical care was extremely low (Table 17).

Similar findings were presented from an American industrial population (SCHOENENBERGER et al., 1972): Of 2725 individuals evaluated as hypertensive, 60% denied prior knowledge of the diagnosis.

Ad 8: DAWBER et al. (1967) stated: "The evidence that the transient elevation of blood pressure immediately produced by caffeine has any cumulative effect on blood pressure level, producing or predisposing to fixed blood pressure elevation, is absent. Examination of the correlation between usual daily coffee intake and systolic blood pressure in the Framingham study failed to reveal any suggestion of an association."

In the Evans County Study (HEYDEN et al., 1972b) the entire population was stratified into two groups, one with regularly "high" coffee consumption (5 cups per day or more) and with "low" or no coffee consumption. White males in the first group had a mean blood pressure of 137/85 mmHg, in the second group 143/88 mmHg; white females 139/85 and 147/88 mmHg, respectively; black males 150/89 and 156/95 mmHg, respectively; black females 155/93 and 162/96 mmHg respectively. This finding of an insignificant but consistently higher blood pressure in all four race-sex groups among persons with low or no coffee consumption – in comparison to high coffee consumers – could be explained by the greater number of overweight persons among non-coffee drinkers. Heavy use of coffee is often associated with heavy cigarette smoking – and cigarette smokers in general tend to have lower average weights than non-smokers.

The effect of caffeine on blood pressure was studied by several pharmacologists. HAUSCHILD and GÖRISCH (1967) reported: "Blood pressure is barely influenced by caffeine; occasionally there is a slight decrease which may be followed by a phase of increased blood pressure." KUSCHINSKY and LÜLLMANN (1972) commented in their textbook of pharmacology: "Caffeine and theophylline in high doses stimulate the vasomotoric and respiratory centers. Nevertheless the blood pressure does not increase because of the peripheral vasodilatation of the skin, kidneys and heart . . . 0.05–0.2 grams of caffeine contained in 1–2 cups of cof-

fee or tea may prevent one from falling asleep. In old aged people or sometimes in patients with hypertension caffeine may paradoxically aid in falling asleep."GOODMAN and GILMAN (1970) made similar comments on beverages with xanthines (e.g. coffee): "Xanthine beverages are often denied to individuals with hypertension because of the action on the cardiovascular and nervous system . . . Most authorities take the attitude that the complete denial of coffee to an individual who enjoys it is apt to be more disturbing than any stimulation he may receive from the beverage. Many patients with hypertension experience neither an increase in blood pressure nor nervousness from xanthine beverages. Indeed, theobromine is sometimes prescribed for its renal and, perhaps coronary effects in such patients. Xanthine beverages accomplish the same end and, in addition, may relieve the headache so common in this syndrome".

This review of epidemiological and pharmacological evidence should remove all misgivings about the use of coffee in hypertensives. Caffeine neither causes hypertension nor aggravates preexisting hypertension.

Summary

Hypertension, even in its mild form, carries a considerable risk for the development of myocardial infarction and stroke. In addition, the hypertensive is at substantial risk to acquire congestive heart failure. Long-term studies using systolic versus diastolic pressure revealed little to suggest a greater role for diastolic pressure as predictor. Casual blood pressure readings as indicator for subsequent blood pressure development in an individual are of great value. In the future, more attention has to be paid to juvenile hypertension. It is alarming that 60% of sustained hypertensives do not know anything about their elevated blood pressures.

Diabetes mellitus

In the Framingham and in the Evans County Studies, hyperglycemia and/or diabetes mellitus range behind hypertension as risk factor for the development of myocardial infarction and cerebrovascular diseases – an obvious contrast to the high risk involved for diabetics in the development of peripheral vascular disease. After 16 years observation, the Framingham group concluded (GORDON et al., 1971): “Glucose intolerance is an important factor in atherosclerotic diseases in all three vascular beds but it is most significantly correlated with the incidence of intermittent claudication. It is in this manifestation of atherosclerosis only that diabetes as an etiological factor becomes comparable with the importance of hypertension for the development of stroke and of hypercholesterolemia for the development of ischemic heart disease.” Neither intermittent claudication nor ischemic heart disease are epidemiologically correlated with obesity. If obesity as a single risk factor is not correlated with these two manifestations of atherosclerosis, we may assume that an additional factor might play some role which, together with diabetes, enhances atherogenesis in all three vascular beds, yet is relatively independent of overweight. In this respect, the prospective Birmingham Study by PEACOCK et al. (1972) showed that only those diabetics who were hypertensive at the same time developed strokes.

In the Du Pont Study the number of hypertensives among persons with diabetes was significantly higher than among age-matched non-diabetics ($p < 0.001$). The higher frequency of hypertension cannot be explained by increasing age or association with obesity (PELL and D'ALONZO, 1967). When classifying all diabetics in 5 different weight groups from the underweight to the most obese, the prevalence of hypertension was greater among the diabetics compared to the non-diabetics in every weight group. The authors summarized their findings:

- “a) The higher prevalence of hypertension among diabetics in comparison to non-diabetics was independent of overweight.
- b) Among the hypertensive diabetics the prevalence of ischemic heart disease was twice as high as among the controls.
- c) Among *normotensive* diabetics there was no difference in ischemic heart disease prevalence in comparison to control persons without diabetes mellitus.

d) The greater susceptibility of diabetics for atherosclerotic heart disease may be explained almost exclusively on the basis of the higher prevalence of hypertension."

The question is raised whether hypertension is already present in the prediabetic state. Is hypertension a potential consequence of clinical diabetes or is hypertension more likely to develop in latent diabetes? The same DuPont Study examined blood pressures in 537 men two years prior to the diagnosis of diabetes mellitus and in 528 men who did not develop diabetes mellitus. In this prediabetic state, blood pressures were found significantly higher among the 537 men who later developed frank diabetes mellitus. The chance to develop diabetes is approximately 63 % greater for persons with elevated blood pressure than for normotensives (PELL and D'ALONZO, 1967).

Co-existence of both hypertension and diabetes mellitus could be a consequence of primary aldosteronism (CONN, 1965). As early as 1910, NEUBAUER showed an interrelationship between diabetes mellitus, obesity and hypertension (DIETERLE et al., 1967). Glucose intolerance was described by DRAZIN in 1953 in *obese* hypertensives. However, in 1967 an observation was reported on *normal weight* hypertensives (DIETERLE et al.). These authors reported that "half of the normal weight patients with elevated blood pressures after a glucose load reacted with a delayed return of plasma glucose to fasting levels. Even in persons with normal glucose tolerance the hypertensive differs from a non-hypertensive by his hyperinsulinism. Our findings suggest an endocrine-metabolic disturbance in essential hypertension."

PAFFENBARGER and WING (1973) confirmed the hypothesis that hypertension, or even a relatively higher blood pressure level, in comparison to normotensive levels during adolescence may be a risk factor for the later development of diabetes. Retrospectively, health records of college students were examined and interval incidence rates of diabetics computed with relation to levels of blood pressure recorded at the time of college case-taking 20 years prior to the diagnosis of diabetes mellitus. Higher levels of systolic blood pressure distinguished the eventual diabetics but diastolic blood pressures did not. "Since obesity predisposes to hypertension, the interval incidence rates of diabetes by combined characteristics of ponderal index and systolic blood pressures were examined . . . Men with both, heavier weight for height and

higher systolic blood pressure in college were at nearly double the risk of adult-onset diabetes over the baseline group with neither excess." As expected, the interval incidence rate of subsequent diabetes among men with a family history of diabetes was 3-fold that found in their colleagues without such background.

Diabetes – as an isolated clinical finding – may be of little influence on the development of manifestations of coronary atherosclerosis. On the other hand the association of diabetes with additional risk factors may be of paramount importance in the etiology of coronary artery disease. KEEN (1972) quotes from a comparison of post-mortem findings between Japanese and American patients with diabetes. This comparison "shows a most striking deficit in the representation of coronary disease as a cause of death in Japanese diabetics (5% of 865) compared with American diabetics (54% of 1283), a difference too large to be accounted for by variation in autopsy methods or criteria. From this, one may conclude that the diabetic is not inevitably condemned to atherosclerotic disease as an integral part of the diabetic syndrome."

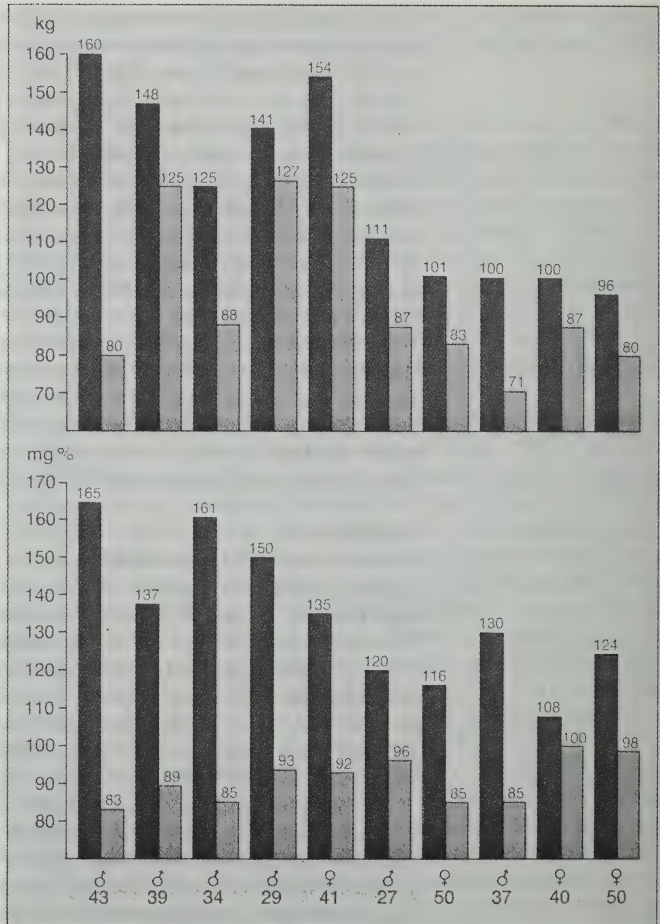
Conclusion

It becomes essential in a diabetic patient to search for associated risk factors, particularly hypertension, smoking, hyperlipoproteinemia type IIb, III, IV and V and hyperuricemia.

Within the available short time a physician can spend with his patient determination of serum lipids assumes equal importance to the determination of blood glucose. At the same time hypertension has to be treated, cigarette smoking abandoned, weight normalized and physical activity increased. Weight reduction alone may eliminate both adult-onset diabetes and essential hypertension (Fig. 21).

Diabetics who reach their normal life expectancy without major vascular complications, mostly belong to the privileged upper social class that has the greater insight into preventive measures, more frequent medical supervision and continuous control of diet, weight and urine sugar. Sociologic-epidemiological studies of the past 20 years indicate that the improved eating patterns, greater attention to weight, and better and more regular medical supervision are indeed more important factors than genetic influences on the natural history of diabetes mellitus. There is no reason to fatalistically assume that vascular complications, in particular microangiopathy, will develop progressively, independent of the quality of diabetes control. In larger series of diabetics under long-term observation, car-

Fig. 21: Weight and diabetes – 10 diabetics prior and after weight reduction (upper half: weight in kg, lower half: fasting blood sugar levels in mg%). Red columns: prior to weight reduction, green columns: after weight reduction. HEYDEN, S. (1970), unpublished.



diovascular and cerebrovascular mortality is definitely higher in patients with poor diabetes control in comparison to patients with very good diabetes control. Good control means avoidance of glycosuria, weight normalisation, non-smoking and optimal treatment of hypertension, if present. GOODKIN has recently shown from the Equitable Life Insurance Company data that weight control,

avoidance of glycosuria and treatment of co-existent hypertension can indeed prevent ischemic heart disease and stroke. Among 1264 diabetics the mortality from these two vascular catastrophies was $2\frac{1}{2}$ times as high in poorly controlled diabetics as in well-controlled diabetics (G. GOODKIN, 1971). Today we are in a similar position as in the treatment of hypertension: According to STRAUSS (1969, and PELL and D'ALONZO, 1970), $\frac{2}{3}$ to $\frac{3}{4}$ of all diabetics are either inadequately treated or not treated at all. This is true not only in university clinics in many Western countries but also in the Joslin Diabetes Clinic in Boston.

Hyperuricemia and Gout

"Gout means the same for the arteries as rheumatism for the heart muscle" (HUCHARD, 1899).

A first epidemiological investigation was published by DAWBER and THOMAS (1968) from the Framingham Study: "A two-fold risk of developing coronary heart disease is found in those with gouty arthritis. A slight upward trend in risk is also seen as the uric acid levels increase in non-gouty patients. These findings suggest that the gouty diathesis, rather than the level of uric acid in the blood, is a factor that increases the risk of CHD." In another paper from the same study (HALL et al., 1967) the development of gout in relation to baseline uric acid levels was shown (Table 18):

Table 18: Relation of serum uric acid levels and gout.
HALL et al., Amer. J. Med. 42 (1967) 27.

Serum uric acid concentrations (first examination)	Development of gout within 12 yrs. of observation
6-6.9 mg%	1.8%
7-7.9 mg%	11.8%
> 8 mg%	36.0%

The association between gout and the development of vascular diseases in the coronary and cerebral arteries has been confirmed in several clinical studies. "Serum uric acid levels of 7.0 mg% or greater is often associated with other factors, such as obesity, hypertension and hyperglycemia. Evidence is available that hyperuricemia operates as an independent risk factor but again further clarification is needed" (STAMLER, 1973).

The frequency with which hyperuricemia is found among overtly healthy persons, is directly related to the prevalence of obesity. An interesting observation was added recently by BABUCKE and MERTZ (1973): "The increase of gout in the Federal Republic of Germany was 20-fold in 1970 compared to 1948." This increase in gout was confined to men and was not seen in women. The mean age of manifestation of gout was 42 years and a peak emerged between age 21 and 30 years! Obesity was found in 69% of the patients.

It has been well known that weight reduction lowers serum uric acid concentrations. Lowering of uric acid levels can reasonably be expected to depend on the amount of weight loss. On the other hand it remains unexplained why a smaller percentage of hyper-

Table 19: Results of weight reduction on serum uric acid levels.

HEYDEN, S. (1970–1972), unpublished.

Group I (n = 49)	Average	Standard Deviation
Age	40 years	12.70
Weight Loss	20 kg	9.71
Basic SUA Levels	8.20 mg%	1.80
Change in SUA Lev.	– 1.56 mg%	1.28%
Group II (n = 18)	Average	Standard Deviation
Age	41 years	13.54
Weight Loss	17 kg	8.63
Basic SUA Levels	7.6 mg%	0.95
Change in SUA Lev.	+ 2.12 mg%	1.66

uricemic patients shows an increase in serum uric acid levels (i. e. not after fasting – but as a long-term effect after many months). In one study (NICHOLLS and SCOTT, 1972) 3 of 15 patients (20%) with hyperuricemia displayed an increase of serum uric acid concentration after weight was normalized; in my own observation of 67 hyperuricemic patients 18 increased from 7.6 mg% to 9.7 mg% (27% of all patients) in spite of an average weight loss of 17 kg! The majority (49 patients with hyperuricemia) showed the expected decrease of serum uric acid levels of 1.56 mg% after a mean weight loss of 20 kg (Table 19).

Conclusion

Weight reduction alone will achieve a significant lowering of pathologic serum uric acid levels. Unexpected (and unexplained) increases of serum uric acid levels in 20 to 27% of patients in spite of weight reduction requires drug treatment.

A high protein diet, including inner organs, alcohol and certain diuretics of the thiazide group have a well-known uric acid elevating effect, and must be taken into consideration.

Obesity

KEYS et al. (1972b) reported from their Seven Country Study of 11,400 men in Northern Europe, Southern Europe and the United States that overweight and obesity make no independent contribution to risk of developing coronary heart disease. "Multivariate analysis of the data showed that no measure of relative weight or obesity made a significant contribution to future coronary heart disease, when the factors of age, blood pressure, serum cholesterol and smoking were comparable." Obesity and even excessive fat accumulation are only indirectly correlated with the development of ischemic heart disease. The connecting link is hypertension. In KEYS' study 60% of the extremely overweight persons were hypertensives. In this 5-year incidence study the Dutch subgroup, for instance, had 86% of cases of ischemic heart disease developing in the heavy overweight group of males (upper 20% of relative weight). But when these men were classified into three blood pressure categories and the data were analyzed considering hypertension and overweight simultaneously, no significant excess risk for the overweight men was found. "The most significant feature is the relationship of blood pressure to relative weight and fat mass". PAUL (1971) – on the basis of the Pooling Project involving 6,640 males – provided further evidence that the heavily overweight men (relative weight >1.21) have the highest percentage of patients with diastolic hypertension (Table 20).

Tab. 20: Diastolic hypertension and obesity.

PAUL, O., Brit. Heart J. 33 (1971) 116.

Diastolic BP (mmHg)	Relative weight		
	< 1.10 (n = 2648)	1.10–1.21 (n = 1821)	> 1.21 (n = 2171)
< 85	67%	53%	39%
85–94	23%	30%	33%
95–104	8%	12%	18%
> 104	2%	5%	10%

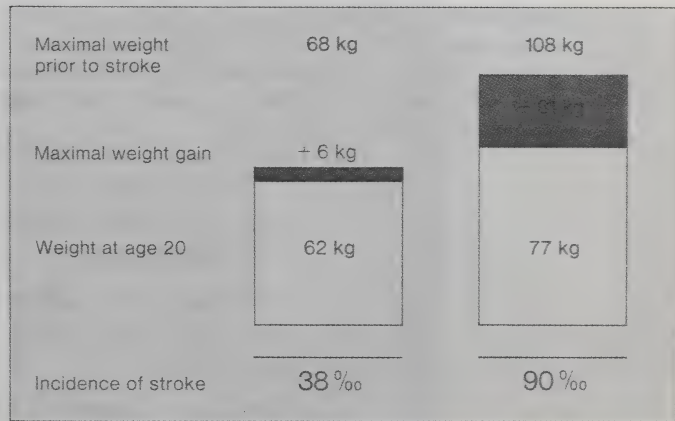
Taking both factors, obesity and hypertension, into consideration, the decisive risk factor remains hypertension. Still, some 40% of extremely obese people do *not* have hypertension.

In addition, we were able to show in the Evans County Study that weight at age 20 is not as important as weight gain after age 20 for

the development of systolic and diastolic hypertension (HEYDEN et al., 1971 b). In view of the importance of sustained hypertension for the development of stroke, the following incidence rates are not surprising. The incidence rate per 1000 within 7 years observation period in males with normal weight at age 20 (below 68 kg) and with little or no weight gain after age 20 was 38/1000. However, in males who were already overweight at age 20 (>68 kg) and who gained at least 14 kg after age 20, the incidence rate was 90/1000 (Fig. 22).

Fig. 22: Age-adjusted incidence rates of non-fatal strokes in males per 1000 according to weight at age 20 and degree of weight gain.

HEYDEN, S., Verhandl. Dtsch. Ges. Inn. Med. 78 (1972) 393.



Weight and myocardial infarction were inversely related; within the same 7 years observation period the incidence rate for the development of myocardial infarction was 76/1000 for males who were normal weight at age 20 and were more or less weight stable after age 20. On the other hand, the incidence rate was 66/1000 for overweight men at age 20 who reported large weight gains after age 20. The Framingham Study also reported on the non-existing association between overweight as a single factor and myocardial infarction. KANNEL et al. (1967 b) stated, however, that angina pectoris was found more frequently among males who were overweight than in normal weight men. Similarly, sudden death was observed more frequently among overweight men in the Framingham Study. Neither KEYS' Seven Country Study nor the Evans County Study were able to confirm this observation.

Tab. 21: Effective treatment of obesity.
HEYDEN et al., Nutr. Metabol. 15 (1973 b) 295.

Medical recommendations
for weight reduction

1. Replacement of sodium by herbs and spices
2. Restriction of carbohydrates to 60 g per day (= 240 calories)
3. Normal protein ingestion of 60 g (= 240 calories)
4. Limitation of fat intake to 25 g (= 225 calories)
5. One fasting day per week. Only non-caloric liquids are permitted
6. Keeping a diary of food intake
7. Daily weight recording in the morning
8. 150 calories for breakfast
150 calories for lunch
400 calories for dinner
9. The sodium restriction may be lifted after 8–10 weeks for persons with normal blood pressure levels.

Conclusion

The epidemiological literature is full of evidence that obesity per se does not have atherogenic properties – if obesity is not associated with hypertension, hypercholesterolemia, hyperuricemia, gout or diabetes (GOFMANN and YOUNG, 1963). GERTLER et al. (1964), discussing the coronary profile, stated, that "weight is an absolutely useless predictor for the development of ischemic heart disease". These observations are, however, not relevant for the development of cerebral infarct. Weight at age 20 and weight gain seem to be an important risk factor for stroke. Essential hypertension is one of the major complications of obesity. The high percentage of 85–90% of diabetics who are overweight speaks for itself. 70% of patients with gout are obese. In hyperlipoproteinemia (type II B, III, IV and V) almost 80% of the patients are overweight. The treatment of obesity should include one fasting day per week and a 700 calorie diet for the remaining week days (Table 21).

Physical inactivity

Previous literature from different epidemiological studies has produced conflicting interpretations on the role of physical activity in preventing I.H.D. Our findings from the Evans County Study of 2500 adults over a 7-9 year period shed new light on the controversial question (CASSEL et al., 1971). Farm owners and share croppers were compared with the following results:

1. A highly significant difference was found in the incidence of myocardial infarction, between share croppers (31/1000) and farm owners (99/1000);
2. Only among share croppers was the white rate (31/1000) as low as the black (39/1000). Significantly, among all the variables explored this is the sole instance in which comparable black and white rates have been discovered;
3. Only the share croppers were excessively physically active, under climatic conditions, at least from March through October, that were sub-tropical. At the time of analysis, farming was still largely without automatisation;
4. Considering all working white males, the following distribution of age-adjusted incidence rates evolved: professionals had similar incidence rates as farm owners (94/1000 and 99/1000, respectively), men working in trades 143/1000, clerks 180/1000, laborers 190/1000, but, as already mentioned, share croppers only 31/1000;
5. In spite of remarkable differences in the incidence rates between non-farm and farm-professions no significant differences were seen in risk factors (hypertension, hypercholesterolemia, obesity). Levels of blood pressure, both systolic and diastolic, were found to be almost identical in the two groups. At each age farmers did tend to have slightly lower cholesterol levels and, rather surprisingly, to be slightly heavier for their height than non-farmers. These differences are minimal, however, and are unlikely to account for the marked differences in incidence rates (which were 150/1000 for non-farmers as compared to 73/1000 for farmers). In contrast to these biological risk factors, there were sizable differences in the proportion smoking cigarettes, with fewer farmers smoking at each age than non-farmers. A separate analysis revealed that smoking increases the risk of coronary heart disease in both farmers and non-farmers; farmers had lower rates than non-farmers whether they smoked or not. We concluded that the

most likely explanation for these findings was that sustained physical activity above a certain critical threshold value may be protective against ischemic heart disease.

Previously it had been suggested that if physical activity is in any way protective against coronary heart disease, its effects are most pronounced in preventing fatal attacks of coronary heart disease. This hypothesis was examined in the Evans County Study comparing mortality rates between physically inactive and physically active professions.

Tab. 22: Coronary heart disease, mortality rates in "active" and "sedentary" non-farm occupations, white men 1960-1962 to 1967-1969.

CASSEL et al., Arch. Int. Med. 128 (1971) 920.

	"Sedentary" occupations: professionals, clerks etc.	"Active" occupations: trades, service and laborers
Number of men examined in 1960/62	138	199
All ages n = mortality (IHD)	10	8
Mortality rates/1000	72.5	40.5

Given the small numbers in each cell and the lack of any gradient in the overall incidence rate, this consistently higher mortality in the "sedentary" occupations is quite impressive and is difficult to explain except on the grounds of variation in some threshold values of physical activity.

"All proponents of physical activity programs for the prevention of ischemic heart disease feel that the most important point in increasing physical activity is the development of coronary collaterals" (KÖNIG, 1973). This hypothesis remains debatable.

HELFANT and GORLIN (1972) took issue with this concept in an extensive editorial: "Collaterals are congenitally determined channels; however, after more than three decades of study, the factors that stimulate their function and the degree to which collaterals protect patients with coronary artery disease remain controversial . . . To date, no systematic study in man shows a correlation between improvement in exercise tolerance and the promotion of coronary collaterals."

Unfortunately, little is known clinically about the degree to which collaterals will protect the patient from subsequent death. In our study, six of 44 patients with angiographic evidence of a functioning collateral circulation died after study compared with 10 deaths in the 45 patients in whom collaterals were angiographically absent. This suggests but does not statistically prove that the presence of collateral vessels may decrease subsequent mortality . . . There is little to support the concept that collaterals prevent the development of acute myocardial infarction. But increasing evidence from post-mortem, arteriographic, and experimental studies suggests that a well-functioning coronary collateral circulation may be an important factor in the ability of at least some patients to *survive* an attack of myocardial ischemia or infarction".

Conclusion

Epidemiological and clinical reports seem to agree on the following observations:

1. *Among the risk factors for the development of myocardial infarction, physical inactivity is regarded as a secondary factor. Conversely, physical activity may be protective if the well-trained person is at the same time a non-smoker, normotensive, non-diabetic and normocholesterolemic.*
2. *MANN et al. (1969) from their own experience with a strenuous physical fitness program categorically state: "Exercise and fitness are minor elements among risk factors for coronary disease or, as we believe, physical fitness also influences coronary heart disease more directly, that is, in ways not reflected by the indirect risk factors measured. There is no substantial basis for supposing that exercise operates through an effect on sterol metabolism, atherogenesis or thrombotic reactions . . . It is surprising that this training, which seems to have been maximal for many of the men, had relatively small effects on risk factors. The increase in serum uric acid is unexplained, glucose tolerance was not improved by training, the fasting serum triglyceride levels were significantly increased and the decreases in relative weight were generally small." There are some reports in the literature that a well-balanced physical fitness program may beneficially influence elevated blood pressures.*
3. *Only extreme physical activity – comparable to the endurance training of professionals – may protect from myocardial infarction. However, the threshold level at which an effect on ischemic heart disease may be operating still needs to be defined.*

4. *A positive effect of regular physical activity has been established in patients with diabetes mellitus. Physical training is but one of the three most important considerations of diabetes therapy: diet, insulin or oral antidiabetics and regular physical training.*
5. *The fact that a well-developed collateral circulation may be beneficial is not being questioned. However, the mechanism how the collateral circulation develops is still unsolved. Collateralisation probably may not be achieved with intensive physical training programs.*
6. *The sum of all presently available facts regarding physical activity point to an increased use of sports, hiking, ball games, bicycle riding, tennis and swimming – for psychological reasons (distraction from overeating, smoking and general relaxation), as well as for the improvement of glucose tolerance in diabetics. Possibly, there is some use of a carefully monitored activity program in the treatment of hypertensive patients. Physical activity is ineffective in lowering cholesterol levels.*

Commentary

Presently no chronic-degenerative diseases are being attacked with the principles of applied epidemiology. Early detection has been limited by the use of traditional clinical tools. An exception is the concept of the coronary risk factor profile which has evolved from two decades of epidemiological research.

EPSTEIN (1973) demonstrated the magnitude of the problem: "Among 1000 men, about 10%, or 100 men will experience a heart attack within the next 10 years. At least a quarter of these manifest as sudden deaths which occur before the patient reaches the hospital. A minimum of 25 deaths, more likely closer to 30, is a conservative figure for deaths within an hour.

Another 75 men will experience a myocardial infarction over the 10-year-period and reach the hospital. Within a month, from 25 to 30% (approx. 20) of the 75 patients will die, mostly within the first few days."

The problem has been to identify these men prior to the clinical event so that preventive measures may be instituted. The risk factor profile has provided the answer. Thirty-eight percent of healthy men have two or all three of the following risk factors: hypercholesterolemia >250 mg %, diastolic hypertension >90 mmHg and cigarette smoking. These 38% generate almost 60%, or close to $\frac{2}{3}$'s, of all subsequent heart attacks!

The data from the Pooling Project are summarized by EPSTEIN (1973) in Table 23. One could take the position of the devil's advocate and point out that more than 40% of men with two or even three risk factors will *not* develop myocardial infarction, at least not within the 10 year observation period. This statement, however, disregards other diseases which are sequelae of the same risk

Tab. 23: Risk factors and incidence of ischemic heart disease in 30-59 year old men during a 10 years observation period.

EPSTEIN, F., *Circulation* 48 (1973) 185.

Risk factors	n (men only)	Ischemic heart disease	Incidence rate/ 10 years
No risk factor	1249	28	20
1 risk factor	3320	171	48
2 risk factors	2178	198	90
3 risk factors	575	82	171
Total	7322	479	-

factors. As has been shown previously, hypertensive patients are predisposed to stroke and congestive heart failure, cigarette smokers to the development of peripheral vascular disease as well as many other diseases associated with chronic cigarette smoking such as chronic bronchitis, bronchogenic cancer, bladder cancer and peptic ulcer.

Health education has assumed a prominent position in medicine. The concept of risk factors will play an important role in bringing together many health professionals who have not traditionally interacted for the benefit of the patient. The physician, health educator, nurse and other paramedical personnel should be developing health education programs for the general population as well as planning health maintenance programs with individual patients. Both of the above must be done to achieve any measure of success with the more difficult task of intervention, especially in the patient who feels healthy, yet has abnormal laboratory values. Predictably, this patient will resist efforts to change habits he enjoys (for example, sitting in front of the television for hours, drinking beer and consuming other empty calories, smoking etc.) as well as life long eating patterns in favor of a more sensible diet. For the diabetic, especially one who is insulin dependent or has to take drugs, a full understanding of his disease and the role of diet is critical. He constantly needs to resist the temptation to use 10 or 20 units of insulin more than prescribed in order to allow himself an extra portion of certain carbohydrates. Physicians will also be combating several nonsensical approaches to diet control which our civilization has developed – one of the most fatuous being the appetite depressing tablet which prevents the obese patient from actively participating in his weight reduction. Similarly, a more natural approach to fluid control is simple sodium restriction or one fast day per week rather than the intake of diuretics many obese patients think they need.

Summary

With the new health consciousness of the general public, many physicians are being confronted with questions on the role of nutrition, smoking, and the need for physical activity in maintaining a healthy living standard. Physicians are better able to answer these questions because of the Framingham Study and similar long-term epidemiologic observations which have clarified the importance of a number of risk factors for the development of degenerative vascular diseases. In the post-Framingham era a ranking order of risk factors for the three main vascular beds has evolved. This enables the physician to choose priorities in diagnostic steps and to plan measures of intervention. The relevant risk factors are applicable to the general population even though the determination of the physical status of any person is difficult. Medicine is not an exact science and people cannot be compared to a table of standards as machinery. Considering these limitations, results of intervention studies have nevertheless strengthened the position of preventive cardiology: It has been proven that removing or modifying risk factors positively affects the course of a number of chronic degenerative diseases. The evidence was first seen in severe hypertension where the mortality rate from stroke decreased and congestive heart failure and renal complications were prevented.

Further evidence has been provided by the lowered risk in ex-smokers for myocardial infarction as well as for intermittent claudication (and bronchogenic cancer). Thirdly, the combination of a well-balanced dietary and drug treatment in diabetes has revealed better survival rates and less morbidity in these patients as long as ideal weight and regular physical activity were maintained. A fourth example of the effectiveness of reducing risk factors can be shown from the dozen long-term experiments in healthy males as well as in patients with myocardial infarction whose diets were changed to lower cholesterol levels. These studies were carried out in many countries and demonstrate the value of dietary changes in primary prevention of myocardial infarction as well as in secondary prevention of re-infarction. The synopsis presented in this review supports the recommendation that risk factor screening and intervention should be introduced in each physician's office. Methodology, concentration of screening procedures on essential tests, definition of normal, borderline and pathological levels are discussed. The prin-

principles of dietary therapy in obesity (for the treatment of hypertension, diabetes and gout) and in hypercholesterolemia are outlined to help the practitioner in motivating his patient with a program of applied epidemiology.

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COMMENT ON GOAL 6

(p. 48-51)

The recommendation by the National Academy of Science (1974) for a three gram a day allowance of salt has, unfortunately, not made the headlines. I agree wholeheartedly with the statement by Drs. Maneely and Battarbee, cited in the U.S. Senate Report, that 3 g Na "is more than enough." The publication of the U.S. Senate Report with its very welcome reiteration of the salt restriction, coincided with the decision by the baby food industry to eliminate salt from their products. This unexpected (but long overdue) development should encourage all of us, in medicine as well as in government, to persuade the food processors to take steps in the same direction as the baby food industry, i.e., to make more use of herbs and spices and decrease the usage of sodium chloride as much as possible. The sentence on p. 48 of the U.S. Senate Report: "Sodium intake is more and more determined by the food processors rather than by the individual" appeared in small print (but deserved large print)! In the Evans County Heart Research Study in Claxton, Georgia (Chairman, Curtis G. Hames, M.D.), some 60 overweight hypertensive patients were placed on a daily intake of 3 g Na Cl and on a weight reducing diet for one year. A control group, matched by age, race, sex, blood pressure elevation, degree of overweight and several biochemical parameters was followed on a regular basis with blood pressure measurements and urged to see their family physicians. At the end of one year an independent observer recorded the blood pressures of all patients. The results were slightly in favor of the salt restriction and weight reduction group since systolic blood pressure levels were significantly lower than those in the control group. There were no differences in diastolic blood pressure levels, i.e., they were lowered in both groups—in the control group on account of increased use of medication; in the diet group, on account of the salt restriction. It should be mentioned that each dieter received (free of charge) a package of potassium salt on a weekly basis to encourage its use by the entire family.

The last chapter of the "nutrition-hypertension" story has not been written yet and promising looking results of basic research on the use of polyunsaturated free fatty acids (PUFA) in the synthesis of prostaglandins have stimulated us to incorporate this approach in an intervention trial for hypertensive adolescents, aged 15-19 years in Carbarus County, North Carolina. It is believed that the increased renal prostaglandin synthesis has a sodium excreting effect. Whether this is true for free living adolescents will be tested. While this hypothesis is highly speculative, a practical "guide to reducing salt consumption" (p. 50) should be developed. A simple listing of foods with different sodium contents appears insufficient. We have, therefore, enclosed a list for the use of herbs and spices in a number of vegetables, salads, etc.

LITERATURE

Heyden, S.; Tyroler, H. A.; Hames, C. G.; Bartel, A.; Thompson, J. W.; Krishan, I. and Rosenthal, T.: Diet Treatment of Obese Hypertensives. *Clin. Sci. Molecular Med.*, 45:209s, 1973.

DIET TREATMENT OF OBESE HYPERTENSIVES

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SUMMARY

1. The management of hypertension in overweight subjects has been studied.
2. Sixty-three patients were randomly allocated into a 'dietary management' or 'treatment' group; the sixty-four controls were told of their hypertension and instructed to seek advice from their usual medical attendant. Reassessment was at 1 year.
3. Treated patients consumed a 700 calorie, 1 g NaCl diet daily.
4. Weight loss was greater in the 'treated' group.
5. The average fall of blood pressure was slightly greater in the 'treated' group.

Key words: obesity, hypertension, weight reduction, salt restriction, intervention study.

This is a 1 year progress report of the Evans County Study of dietary management of elevated blood pressure in overweight individuals.

Evans County is a predominantly rural, biracial county, within the high cardiovascular disease belt, which extends along the coastal plain of the eastern seaboard of the United States. This community has been the locus of ongoing cardiovascular epidemiological studies, under the direction of one of us (C.G.H.) for the past 13 years. The subjects for the experiment reported here were drawn from the survivors of a community prevalence study initiated in 1960. We have documented a high prevalence of elevated blood pressure in Evans County in these studies.

Of the adults, 31% in 1969 had elevated diastolic pressure (i.e. repeated casual diastolic blood pressure readings equal to or greater than 95 mmHg). The prevalence is considerably higher in blacks than whites; for adults 43% of blacks contrasted with 23% of whites.

Approximately half of the subjects with elevated diastolic blood pressure were significantly overweight, and these individuals constituted the target, community-based, population. All subjects over age 65, and patients of any age with either history or clinical evidence of coronary heart disease or stroke, were excluded from this study.

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Eligible study subjects were re-examined in June 1971 and then half were randomly allocated into a dietary management or treatment group; subjects randomly allocated to the control or comparison group were told of their elevated pressure and advised to seek treatment through their usual medical care source.

The dietary experiment under the direction of S.H. consisted of a low calorie, low salt diet providing 700 calories/day from approx. 50 g of carbohydrates, 60 g of protein, 30 g of fat, with a goal intake of about 1 g of NaCl daily. Potassium-containing salt supplements were given out free of charge.

For very obese, physically inactive individuals this is essentially a maintenance rather than a weight reduction diet. Therefore, according to the initial degree of obesity and physical activity, between 1 and 3 days of intermittent fasting per week were recommended, allowing *ad libitum* intake of non-calorific liquids.

Instruction was provided both in group and individual sessions with S.H. and a local resident trained as a health auxiliary. Weekly visits were scheduled for blood pressure measurements, review of weight and diet status for the first 2-4 months of the programme and then spaced once a month and finally once every 2 months when casual blood pressure was below 90 mmHg.

The randomization process provided sixty-three subjects in the weight reduction group and sixty-four in the control group. The two groups were most similar with respect to their age, blood pressure, weight indices and history of drug therapy at intake. The average age of the population was 54 years, average systolic blood pressure 167 mmHg, and average diastolic blood pressure 102. The relative weight of the population was 156%, i.e. as a group they averaged 56% above their 'ideal' weight based on the Metropolitan Life Insurance standard. The subjects in both the treatment and control group were of approximately the same race-sex composition, with black females most numerous, followed by white females, white males and black males. The mean relative weight was highest in the black females. They averaged 68% above the ideal weight for their height. White females were 59%, and white and black males approx. 35%, above the ideal weight.

The progress of these two groups of subjects during a 1 year follow-up is summarized in Fig. 1.

It will be noted that there was a sizable reduction in weight in the treatment group from an average of approx. 88.5 kg (195 lb) to a final weight of approx. 80.3 kg (177 lb), representing an average loss of approx. 8.2 kg (18 lb) per subject. There was much less evidence of weight reduction in the control group, a decline from an intake of 89.4-87.5 kg (197-193 lb). Parallel decreases in blood pressure occurred in these two groups, and at 1 year follow-up an independent observer, unaware of which subject was in the treatment and which in the control group, produced blood pressure measurements indicating a decline of 18 mmHg systolic pressure in the treatment group, and 12 mmHg in the control group, and an average diastolic decrease of 13 mmHg in the treatment group and 8 mmHg in the control group.

Some of the decline in blood pressure for both treatment and control groups can probably be attributed to the psychological effects of intensive follow-up with familiarization with the blood pressure measuring procedures. Some of the decrease in the control group is more likely attributable to changes in medication usage. At intake there were twenty-eight subjects in the treatment group and twenty-seven in the control group using anti-hypertensive medication. Over the year period of this community-based experiment the number of subjects in the dietary management group using anti-hypertensive drugs declined to eighteen, whereas the number in

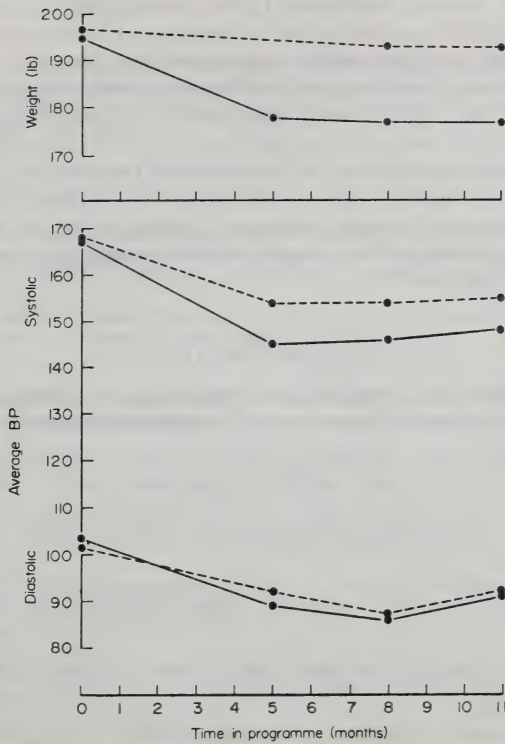


FIG. 1. Change in weight and blood pressure during the first year of the programme. —, Treatment; ----, control.

the control group using anti-hypertensive drugs increased to thirty-six. The fact that some differences in the blood pressure of subjects in the treatment and control group persisted despite this changing drug utilization lends credence to the impact of the dietary programme in achieving blood pressure reduction. The fact that weight reduction alone is not the total explanation for the blood pressure reduction in the dietary treatment group was made apparent by consideration of the association between weight reduction and blood pressure change.

Although there was a statistically significant association, the correlation coefficient is small (0.25) and therefore weight reduction *per se* statistically explains only a small proportion of all the blood pressure change. Alternative explanations, in addition to the psychotherapeutic benefits of the instructional programme, and the procedural familiarization effect previously alluded to, include the benefits of salt restriction and the possible hypotensive effect of the use of potassium supplements.

This experiment has demonstrated that subjects in a free-living community who are both overweight and have elevated blood pressure, but are otherwise healthy, can be screened and

recruited into a weight reduction programme. Of sixty-three subjects so randomized into the dietary programme fifty-eight remained in that programme for 1 year, and sixty-two of sixty-four in the control group were followed for the same period of time.

Obviously, longer periods of observation are necessary to determine the long-term effectiveness of a programme of this type, including compliance, successful maintenance of a diet, and ultimately the impact, if any, on morbidity and mortality. The experience reported to date is but the first pilot phase of a large-scale community blood pressure intervention programme. Obviously, no measures of health impact can be reported at this time. It does seem apparent, however, that satisfactory participation, compliance, and successful, measurable, blood pressure reduction has been achieved for a 1 year period in obese, asymptomatic hypertensives given the regimen identified here.

ACKNOWLEDGMENT

This work was performed as a feasibility and pilot study with contract support from the NHLI as part of the Hypertension Detection and Stepped Care Program.

HERB AND SPICE LIST

- ALLSPICE:** Fruit compote, pumpkin, meat loaf, meat balls, beef, lamb, chicken, turkey, duck, fruit and cabbage salads, poached fish, beets, carrots, parsnips, turnips, spinach, winter squash.
- ANISE:** Fruit juice, fruit cup, shellfish, cottage cheese, fruit compote, baked apple, braised chicken.
- CARAWAY SEED:** Tomato juice, cottage cheese, pork, beef, cole slaw, cucumber, tomato, broiled fish, crab, lobster, poached fish, cabbage, potato, carrots, celery, onions, turnips.
- CAYANNE:** Broiled chicken, tomato, boiled shrimp, broiled shrimp, lobster, crabmeat, cabbage, collard greens, turnip greens, kale.
- CELERY SEED:** Tomato juice, meat loaf, cole slaw, beets, tomato sauce cabbage, cucumbers.
- CHILI POWDER:** Tomato juice, cottage cheese, ground beef, poultry, shrimp, lobster, fish, eggplant, onions, tomatoes.
- CINNAMON:** Fruit compote, fruit salad, applesauce, beets, carrots, onion, pumpkin, winter squash, tomatoes.
- CLOVES:** Tomato juice, cranberry juice, fruit compote, pork, spiced fruit, applesauce, beets, carrots, onions, pumpkin, winter squash.
- CURRY POWDER:** Cottage cheese, pork, lamb, meat balls, meat loaf, seafood, beets, carrots, parsnips, turnips, winter squash.
- DILL SEED:** Tomato juice, vegetable juice, cottage cheese, lamb, fish,
- GINGER:** Apple juice, prune juice, cantaloupe, roast chicken, carrots, winter squash.
- MACE:** Meat loaf, veal chops, broccoli, brussels sprouts, cabbage, snap beans.
- MUSTARD:** Shrimp, ham, pork, ground beef, beets, braised lettuce, cabbage, cucumbers.
- NUTMEG:** Tomatoes, beans, corn, eggplant, onions, ground beef.
- PAPRIKA:** Garnish, cauliflower, corn, spinach.
- PEPPER:** All vegetable juices, all egg dishes, all meat dishes, all poultry dishes, all vegetable salads, all meat salads, all seafood salads, all vegetables.
(black)
(white)

HERB AND SPICE LIST

- BASIL: Tomato juice, vegetable juice, beef, lamb, veal, fish, shrimp, lobster, crabmeat, asparagus, beets, broccoli, cabbage, carrots, celery, cucumbers, eggplant, peas, tomatoes, turnip, spinach.
- BAY LEAF: Tomato juice, tomato sauce, poached fish, shrimp, lobster, beef, lamb and veal stew.
- MARJORAM: Tomato juice, meat loaf, pot roast, crabmeat, fish, shrimp, tomato sauce, celery, collard greens, turnips, turnip greens, onions, peas, potatoes.
- MINT: Fruit cup, fruit juice, melon balls, cole slaw, fruit salad, carrots, peas.
- OREGANO: Tomato juice, vegetable juice, ground beef, pork, lamb, tomato salads, meat salads, vegetable salads, tomato sauce, broiled fish, broiled shrimp, broccoli, eggplant, cabbage, tomatoes.
- PARSLEY: Tomato juice, cottage cheese, meat loaf, all vegetable and meat salads, beets, cabbage, carrots, cauliflower, celery, onions, potatoes, turnip, eggplant.
- POULTRY SEASONING: Ground beef, turkey or chicken salad, chicken, turkey, broiled fish, onions, potatoes.
- ROSEMARY: Fruit cup, pot roast, roast lamb, chicken, turkey, fish, scallops, cauliflower, potatoes, turnips.
- SAFFRON: Rice, chicken, duck, turkey fish, shrimp.
- SAGE: Tomato juice, pork dishes, veal dishes, chicken, turkey, baked fish, beets, celery, onions, summer squash, zucchini squash, tomatoes.
- TARRAGON: Tomato juice, fruit juice, lamb, veal, chicken, turkey, fish, shrimp, green salads, tomato, beets, carrots, summer squash, zucchini squash, string beans, onions.
- SAVORY: Tomato juice, vegetable juice, ground beef, beef, pork, lamb, veal, chicken, turkey, broiled fish, beans, cucumbers, potatoes, tomatoes, carrots.
- THYME: Tomato juice, cottage cheese, eggs, meat loaf, roast beef, roast veal, roast pork, roast lamb, salads, tuna, fish, scallops, crabmeat, lobster, shrimp, beets, carrots, onions, potatoes, mushrooms, summer squash, zucchini squash.

COMMENT ON APPENDIX A

(Table 1)

Table 1 on p. 73 deserves a special comment. Aside from the unfortunate use of the word Negro for black on five occasions, it seems that a gross underestimation of the potential benefit and, in other diseases, a gross overestimation of such beneficial effects from dietary changes has taken place. A case in point is "the potential savings from improved diet", amounting to eight million people=50 percent of all U.S. citizens afflicted with arthritis. How diet could either prevent, improve or cure "arthritis" has never been told. Another massive error was made when it was stated that "20 percent fewer people will be blind or need corrective lenses with improved diets." The huge number of young and middle aged Americans who need glasses would be grateful if dietary advice could be presented which would abolish need for corrective lenses. (We are talking about the 86 million people over three years who wore corrective lenses in 1966, not about the small number of severe diabetic or hypertensive patients whose blindness indeed could be prevented by proper diets.) On the other hand, it appears likely that more than 25 percent of acute digestive conditions might be preventable by appropriate dietary changes. Why only 33 percent of patients with alcoholism can be cured "by improved diet" is difficult to understand. If we are discussing "potential savings", we may be able to save 100 percent of all alcoholics simply by removing the source of their disease. This entire table should either be re-done after careful elaboration with nutritionists and physicians or should be eliminated from the U.S. Senate Report.

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U.S. Senate, Select Committee on Nutrition and Human Needs,
Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you for the letter of May 2, 1977 and for the copy of your publication, *Dietary Goals for the United States*. I have read it with great interest. I was one of those who responded to Doctor Norum's survey and have been interested in nutritional questions for a long time. In agreement with you, I feel that a recommendation can be, and should be, made for a general dietary change in the United States. My recommendations would, in general, be similar to those given in your publication, but let me state my own views briefly.

1. *Caloric restriction (or weight reduction)*.—It should be the goal of every person to achieve his ideal body weight. Caloric restriction in people who are overweight will usually decrease cholesterol and fats (triglycerides) in the blood, the blood pressure, and the risk for gallstones and other diseases. These beneficial effects will be achieved regardless of what diet is used for weight reduction, but I would recommend that at least 40 gms of protein be maintained even with caloric restriction.

2. *Restriction of alcohol intake.*—Alcohol represents a rich source of calories that can contribute significantly to obesity. Also, in many people, it raises blood triglycerides and possibly cholesterol. These adverse effects can occur even with consistent intakes of “moderate” amounts of alcohol. The severe consequences of more excessive alcohol abuse are, of course, well-known.

3. *Reduction in intake of animal fats.*—These fats are rich in saturated fats and cholesterol, both of which raise blood cholesterol. Decreased intake of animal fats will lower cholesterol in most people, and I would recommend this change as far as possible. Hydrogenated vegetable oils are also saturated and have the same effects on blood cholesterol as animal fats. Your recommendation that saturated fats be decreased to 10 percent (or less) of total calories is a good one.

When saturated fats are removed from the diet, they must be replaced with another form of calories (to maintain caloric balance). This can be done with either carbohydrates or vegetable fats. There is presently some controversy as to which would be preferable. Each has its advantages and disadvantages. I will review each briefly.

(a) *Carbohydrate replacement.*—The replacement of saturated fats largely with carbohydrates has the following advantages: 1) carbohydrate-containing foods are more readily available and are cheaper than those rich in vegetable (polyunsaturated) fats; 2) it is easier for the average person in today's society to exchange carbohydrate for saturated fat without causing a marked disruption in his eating habits; and 3) there are no recognized serious hazards of prolonged ingestion of low fat-high carbohydrate diets.

The only possible exceptions to the latter statement are the acceleration of tooth decay, which may follow ingestion of too much simple sugar, and an increase in blood triglycerides in some people. The danger of tooth decay may be reduced somewhat by use of complex carbohydrates rather than simple sugars. The threat of increased blood triglycerides is not thought to be as serious as once considered. Most studies show that the production of high triglycerides is usually transitory. However, some people with familiar increases of triglycerides might be advised not to greatly increase their carbohydrate intake. A final disadvantage of carbohydrates is that they do not decrease the blood cholesterol as much as do polyunsaturated fats.

b. *Polyunsaturated fats.*—Replacement of saturated fats with polyunsaturated has these advantages: 1) they cause a greater lowering of blood cholesterol and triglycerides than carbohydrates; 2) they have been shown in field trials to reduce the incidence of coronary heart disease which has not been shown with high carbohydrate diets. However, these fats are relatively scarce and expensive, and it would probably be impossible to incorporate large quantities into the diet of almost all people. Another possible disadvantage is that the long term effects of high intakes of polyunsaturated fats are not known. To my knowledge no large population groups have ever ingested appreciable quantities of polyunsaturated fats for prolonged periods, and hence there is the remote possibility that the incidence of cancer, neurological disease, etc. might be increased. Nevertheless, the potential benefit in reduction of atherosclerosis would have to be weighed against possible side effects.

In summary, low fat-high carbohydrate diets are probably more practical to achieve for the general population, but they might be less potent for decreasing the incidence of atherosclerotic diseases (heart attack and stroke). The aim is to achieve a reduction in risk factors (high blood pressure and high blood cholesterol, and possibly triglycerides). Thus, at the same time recommendations for dietary change are made, it is equally important to emphasize that people should know how they personally stand with regard to risk factors. What specifically is a given person's blood cholesterol and triglyceride? What is his blood pressure? If either are significantly increased, dietary change may not be enough. Drug treatment may be required. I have seen too many patients who have tried strenuously to control their risk factors by diet when dietary change was insufficient. Therefore, I would urge you to include in your recommendations that each person should know his own levels of blood pressure and blood lipids. Every person must take some responsibility for his own health; and since most physicians are either too busy or too ill-informed about risk factors, a major effort must be made to educate the public on the importance of being concerned about their own risk factors.

Sincerely yours,

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Professor of Medicine.

UNIVERSITY OF CALIFORNIA, SAN DIEGO,
 DEPARTMENT OF MEDICINE,
La Jolla, Calif., August 12, 1977.

HON. GEORGE MCGOVERN,
*U.S. Senate, Select Committee on Nutrition and Human Needs,
 Washington, D.C.*

DEAR SENATOR MCGOVERN: On May 23, 1977, I wrote you in response to your sending me a copy of your publication, "Dietary Goals for the United States." Since that time, I have had further thoughts on the way in which recommendations should be made for dietary changes in the United States. My additional thoughts represent an expansion of the ideas expressed in the last paragraph of my letter.

As I stated, the main purpose of dietary change is to produce a decrease in the incidence of atherosclerotic diseases (heart attack and stroke). The aim is to achieve a reduction in risk factors for atherosclerosis, which are high blood pressure, high blood cholesterol, and possibly high triglycerides. While hypertension and hypercholesterolemia are generally considered to be important risk factors for atherosclerosis, I should say at the outset that it remains to be proven that reduction of either blood pressure or blood cholesterol will actually prevent or retard development of atherosclerosis. For this reason, there is need for ongoing clinical trials to firmly establish the efficacy of reducing risk factors. Until it has been proven that reduction of risk factors, with diet or by any other means, will actually decrease heart attacks or strokes, it will be difficult to make rational recommendations for dietary change. For these reasons, I hope that your committee will take the stance that continued studies are needed to prove once

and for all whether alteration of risk factors will affect atherosclerosis.

Since recommendations for dietary changes are made for the purpose of reducing risk factors, it is most rational that dietary alteration should be considered primarily for those at greatest risk. For instance, people with high cholesterol levels should be urged to alter their diet more than those with low cholesterol. This approach is standard for treatment of hypertension; patients with highest levels of blood pressure are treated more vigorously than those with only mild hypertension. Thus, to a significant extent, reduction of risk factors is a problem of medical therapy. The same holds true for both blood cholesterol and blood pressure. In my opinion, any recommendations for dietary change should clearly spell out the purpose of the change, as for example, to lower blood cholesterol so as to retard atherosclerosis. Also, recommendations that people change their diet should be made only in conjunction with recommendations that they find out their own status with regard to blood cholesterol and blood pressure. In other words, the medical community should not be left out of the equation. While I hold that it is the responsibility of every person to be informed about his own level of risk, the means of altering this risk cannot be entirely divorced from medical therapy.

One problem with making a general recommendation for dietary change, without regard for individual considerations, is the following: First, there is a very large segment of the general population which does not have elevated cholesterol levels. Indeed, many people have low cholesterol levels, and epidemiological studies suggest that they are not at great risk. The height at which cholesterol in blood becomes a significant risk factor has not been defined with precision, but from large studies, evidence suggests that 25-40 percent of the U.S. population is at relatively low risk for heart attack or stroke.

Thus, at both ends of the spectrum, the recommended dietary changes will either be insufficient or unnecessary. In both cases, measurements of blood cholesterol would be helpful in making decisions about individual needs. This is the reason I would urge you to link the need for medical checks for risk with general recommendations of dietary change.

Finally, there is a group of people in the middle who have cholesterol levels that are mildly elevated which may indeed confer an increased risk for atherosclerosis. A strong case can be made for attempting to lower their cholesterol (but let me reemphasize that more investigations are needed for proof). In these people, it may be prudent to alter the diet. The approach could be similar to that which I previously outlined: (a) weight reduction to ideal weight (b) decrease excess intake of alcohol (c) decrease in intake of cholesterol and saturated fats and (d) replacement of saturated fat calories with either carbohydrate, polyunsaturated fats, or both. From what is known today, the value of dietary change can be best judged by observation of changes in blood cholesterol. In those people who are very "dietary responsive" and show a marked fall in cholesterol levels, the dietary change may be beneficial. On the other hand, in people who are "dietary resistant" changes in diet may be of little value. Again, only by actual measurement of blood cholesterol can one determine the response.

From these statements, I hope that you can visualize the complexity of the atherosclerosis problem and how little solid information is available on the value of dietary change. I still maintain that certain suggestions can be made about diet, but I also feel that they should be made in the context of the overall problem of the pathogenesis and treatment of atherosclerosis and in view of great individual variability in the population.

Sincerely yours,

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Enclosure.

Treatment of hypercholesterolemia¹

Scott M. Grundy

A relationship between plasma cholesterol concentrations and development of atherosclerosis is well established. This correlation has been shown in both experimental animals and in man. In a variety of animal species, cholesterol feeding produces hypercholesterolemia that is followed by development of atherosclerosis; in most instances, the degree of atherosclerosis parallels the rise in plasma cholesterol (1). The relation between plasma cholesterol and atherosclerosis also has been demonstrated in several ways for man. In populations in which plasma cholesterol levels are relatively high, the incidence of atherosclerotic disease is greater than in populations with low cholesterol concentrations (2). Within populations, such as that of the United States, atherosclerosis is manifest much more frequently in subjects whose cholesterol levels are high as compared to those with low levels (3-5). These correlations have been shown many times, both prospectively and retrospectively. Also, in patients with familial hyperlipidemias, especially familial hypercholesterolemia, the risk for development of atherosclerotic complications is extremely high (6-8). Therefore, there is little question that high levels of plasma cholesterol are a risk factor for atherosclerosis; this relationship has been amply confirmed.

The next question, of course, is whether a lowering of plasma cholesterol at some point during one's lifetime will retard atherogenesis or reverse existing atherosclerotic plaques. Although this question has not been resolved with certainty, there are several lines of evidence which may justify attempts to lower cholesterol levels in particular patients with hypercholesterolemia.

First, as indicated above, data from various population studies including patients

with familial hypercholesterolemia indicate that high levels of plasma cholesterol are associated with increased atherosclerosis. This finding has led to speculation "that reducing the level of plasma cholesterol in an individual or in a population group will lead to a reduction in the risk of suffering a new event of coronary heart disease" (the lipid hypothesis) (9). Although this hypothesis remains to be proven, circumstantial evidence based on population studies is great and affords considerable rationale for treatment of hypercholesterolemia.

Second, attempts have been made to test the lipid hypothesis in field trials using both diets and drugs to lower plasma cholesterol levels. Indeed, several field trials strongly suggest that lowering plasma cholesterol will decrease clinical manifestations of atherosclerosis (10-13). While the validity of data from these trials has been open to question because of the weaknesses in experimental design (9, 14), this approach may offer the best test of the lipid hypothesis. Recently, the controversial Coronary Drug Project (15) represented a major effort in this direction; unfortunately, the overall degree of cholesterol lowering was small and the results were equivocal. Other large studies, in which the experimental design has been improved, are currently underway or are in planning stages. These studies may provide more direct evidence for or against the lipid hypothesis.

Third, several investigations have demonstrated that diets and drugs used in treatment of hypercholesterolemia can cause regression of xanthomatosis. For example, cholestyramine therapy has been shown to reduce the size of xanthoma in patients with

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familial hypercholesterolemia (16, 17). Cholesterol accumulations in atherosclerotic plaques resemble those found in xanthomas, especially accumulations in tendons; therefore, the mobilization of cholesterol from xanthomas could reflect the occurrence of a similar process in the arterial wall.

Fourth, a more direct approach to the evaluation of therapy would be to visualize changes in the degree of atherosclerosis with arteriography. A preliminary report by Buchwald et al. (18) illustrate this method; in this study, treatment of three patients with hypercholesterolemia by the ileal exclusion operation caused an apparent regression of coronary atherosclerosis.

Fifth, justification for therapy of hypercholesterolemia can be derived from studies in animals. Reversal of hypercholesterolemia by diet or drugs has been shown to cause regression of atheroma in pigeons (19), dogs (20), and monkeys (21, 22). The finding that atherosclerosis can be reversed in mammalian species is of particular interest because their lesions closely resemble those found in man.

Despite these different lines of evidence, many investigators remain unconvinced that induced lowering of plasma cholesterol will actually prevent atherosclerosis. Thus, more studies will be required before the value of treatment of hypercholesterolemia has been shown beyond a reasonable doubt. Nevertheless, the physician is frequently faced with a particular patient who has an elevated plasma cholesterol, and a decision must be made whether to treat the patient or not. Lack of evidence from therapeutic trials does not necessarily interdict treatment of patients with hypercholesterolemia (9); uncertainty may exist, but a decision must often be made. Indeed, it is the contention of many investigators, including the present author, that the weight of the evidence, both from epidemiological and experimental studies, justifies efforts to lower plasma cholesterol. While future clinical trials may modify this contention, arguments can be made from the evidence cited above to support the concept that it is reasonable to treat hypercholesterolemia in an attempt to retard atherosclerosis.

Definition of hypercholesterolemia

Abnormally high cholesterol concentrations (hypercholesterolemia) can be defined in either of two ways: 1) as concentrations in the upper 5 to 10% of a given population, or 2) as plasma levels that are associated with an increased risk of atherosclerosis. While the former method is in common usage today, the latter is of more practical clinical value. In most instances, the concentration of cholesterol in plasma is of interest only insofar as it is a risk factor for atherosclerosis. Thus, according to a normal distribution curve, concentrations greater than the 90th percentile for most populations in the United States are usually greater than 275 mg/dl (23). However, as clearly shown by the Framingham study (4, 23), even below 275 mg/dl there is a correlation between the level of cholesterol and the incidence of atherosclerotic disease. For example, the Framingham male population whose plasma cholesterol was less than 190 mg/dl had only half the chance for developing coronary heart disease as those with concentrations of 190 to 250 mg/dl. Therefore, it is eminently logical to conclude that cholesterol levels in the latter group were not entirely normal. Since there appears to be a graded relationship between cholesterol levels and atherosclerosis, hypercholesterolemia will be defined somewhat arbitrarily in this paper according to degrees of severity, i.e., mild, moderate, and severe; this categorization may prove useful for understanding both the causes and the best mode of therapy of elevated plasma cholesterol.

Mild hypercholesterolemia

For present purposes, mild hypercholesterolemia can be defined as plasma cholesterol concentrations of 225 to 275 mg/dl. The causes of mild hypercholesterolemia have not been explored adequately. Undoubtedly, both environmental and genetic factors play important roles. Some of the environmental factors that may contribute to mild elevations of cholesterol are diet, obesity, lack of exercise, stress, and possibly smoking. Diets rich in saturated fats and cholesterol are almost certainly responsible for a part of the increase in the average level of cholesterol in our population. While

other environmental factors could contribute to a higher plasma cholesterol, genetic factors may be implicated as well. Recently, considerable interest has centered on the role of heredity in the development of more severe forms of hypercholesterolemia (24-26), but milder forms of hypercholesterolemia are probably induced, in part at least, by hereditary influences. Thus, additional epidemiological studies are needed to dissect the relative importance of genetic and environmental factors in milder forms of hypercholesterolemia.

As shown in Framingham (4, 23), most patients with clinical atherosclerotic disease fall into our category of mild hypercholesterolemia; therefore, considering the whole problem of the relationship between plasma cholesterol and atherogenesis, the vast population with mild hypercholesterolemia must not be overlooked. If a significant reduction in atherosclerosis through cholesterol lowering is going to be achieved in the general population, preventive measures will have to be extended to those subjects who we would classify as having mild hypercholesterolemia.

In patients with milder forms of hypercholesterolemia, excess of plasma cholesterol may reside in several different lipoprotein fractions. When the increment occurs in low density lipoproteins (LDL), the patient is probably at greatest risk because LDL is considered to be the most "atherogenic" of all the lipoprotein fractions. In some patients, who also have hypertriglyceridemia, the increase in cholesterol is found in very low density lipoproteins (VLDL). Whether increases in VLDL per se are associated with an increased atherosclerosis is presently a subject of controversy (27-30); one cause for this controversy may be related to the quantity of cholesterol in total plasma and VLDL. When total plasma cholesterol concentrations are in the ideal range (i.e., less than 200 mg/dl), increases in triglycerides with VLDL may not confer a greater risk (24, 30). Thus, the amount of cholesterol in plasma could be more significant for atherogenesis than the triglyceride level. Finally, patients who show increases of cholesterol levels in high density lipoproteins (HDL) may actually be protected from ath-

erosclerosis (30, 31). The mechanism of this protective effect has not been elucidated, but it has been suggested that HDL plays a role in the mobilization of cholesterol from tissues; another possibility is that HDL partially blocks the uptake of LDL by tissue (32). By either mechanism HDL could reduce cholesterol concentrations in arterial tissue.

For treatment of hypercholesterolemia, two modes of therapy are currently available—diets and drugs. In the case of mild hypercholesterolemia, dietary treatment is usually preferable. An important form of dietary therapy is weight reduction. It has been shown that weight loss can cause a lowering of the plasma cholesterol, especially cholesterol in the VLDL fraction (33,34). Whether caloric restriction also causes a decrease in LDL levels has not been determined with certainty, but this clearly is an important question for further investigation.

Another line of dietary therapy is to reduce the quantity of animal fat consumed. Removal of animal fats from the diet decreases intakes of both cholesterol and saturated fats, and both are known to increase plasma cholesterol concentrations. When animal fats are reduced we must ask how the calories should be replaced; specifically, should they be replaced largely with carbohydrate or with polyunsaturated fats? While either change can cause a reduction in plasma cholesterol, replacement with polyunsaturated fats will usually produce the greater lowering. However, large quantities of polyunsaturated fats must be ingested each day to cause a marked lowering in cholesterol; thus, if saturated fats can be replaced entirely by polyunsaturated fats a reduction in cholesterol concentrations of 25 to 30% may be expected (35), but with lesser quantities of polyunsaturated fats, the decrease in cholesterol will be correspondingly less.

The mechanism of cholesterol lowering by polyunsaturated fats is a question of considerable importance and controversy. In patients with mild elevations of cholesterol, either with or without increases in plasma triglycerides, these fats frequently cause an increased excretion of cholesterol (or bile

acids) simultaneously with the decrease in plasma cholesterol (36-40). Whether increased excretion of cholesterol is associated with a mobilization of cholesterol from tissue pools has not been determined. Recent studies on effects of polyunsaturated fats on lipoprotein turnover suggest that they inhibit hepatic secretion of LDL (41).

Several field trials (10, 11, 42-44) have been carried out to test whether polyunsaturated fats will decrease the risk for coronary heart disease. Most of the subjects in these studies would be classified as having mild hypercholesterolemia. While the experimental design of these trials has been justly criticized (9, 4), the results are nevertheless suggestive that polyunsaturated fats reduce risk. Also, diets rich in these fats are usually well tolerated, and no serious side effects of their long-term ingestion has been proven. Although many authorities are not yet willing to recommend whole scale alterations in American and European diets (9), there appears to be no significant danger in the use of polyunsaturated fats to lower plasma cholesterol.

For most patients with mild hypercholesterolemia, widespread drug treatment probably can not be justified at the present time. In the future, with the development of new drugs that are more effective and safer than those presently at hand, drug therapy of mild hypercholesterolemia may become more practical. However, there is one agent which may be considered for patients with milder forms of hypercholesterolemia; this is β -sitosterol. β -Sitosterol is a natural sterol in plant foods, and when given in large quantities it blocks intestinal absorption of cholesterol thereby causing a reduction in plasma cholesterol levels. Recent studies from our laboratory indicate that a maximum reduction in cholesterol absorption can be achieved at intakes of about 3 g per day (45): this intake is considerably lower than was previously thought necessary to achieve full effects (46, 47). Because β -sitosterol is active only in the lumen of the intestine and is itself not absorbed to a significant extent, it is considered to be almost completely safe. Therefore, β -sitosterol may prove to be a useful supplement to diet in the treatment of mild hypercholesterolemia.

Moderate hypercholesterolemia

Plasma cholesterol levels greater than 275 mg/dl are abnormal by almost any criteria. For this discussion, moderate hypercholesterolemia is defined as plasma concentrations in the range of 275 to 350 mg/dl. At these concentrations, the risk for atherosclerotic disease is far greater than with cholesterol levels below 200 mg/dl (4, 23).

In patients with moderate hypercholesterolemia, dietary factors undoubtedly can contribute to the increased levels of cholesterol; thus, the ingestion of diets rich in saturated fats and cholesterol may well increase cholesterol concentrations into this higher range. Indeed, many patients with moderate hypercholesterolemia are particularly "dietary responsive," and removing saturated fats and cholesterol, and replacing them with polyunsaturated fats, can cause cholesterol concentrations to fall to near or below 200 mg/dl.

Although some patients with moderate hypercholesterolemia are especially dietary responsive, hereditary factors frequently contribute to high levels of cholesterol in this group. Indeed, at least two monogenic disorders have been identified which induce hypercholesterolemia; these are familial combined hyperlipidemia and familial hypercholesterolemia (24-26). Also, multiple genetic factors may combine to cause elevated cholesterol levels (polygenic hypercholesterolemia) (25, 26). The monogenic disorder, familial combined hyperlipidemia, and the polygenic forms are probably the most common causes of moderate hypercholesterolemia. Although a single gene defect seems to predominate in familial combined hyperlipidemia, several different lipoprotein patterns can occur within afflicted families; some family members show pure hypercholesterolemia, some have pure hypertriglyceridemia, and others have combined hyperlipidemia (25, 26). In other patients with moderate hypercholesterolemia several factors appear to interact to cause high levels of cholesterol; while some of these factors may be environmental, examination of relatives of these patients suggest that multiple hereditary influences are involved, hence the designation polygenic hypercholesterolemia (25, 26). In both famil-

ial combined hyperlipidemia and polygenic hypercholesterolemia, the risk for atherosclerosis appears to be increased. However, these patients rarely have xanthomatosis, as typically found in familial hypercholesterolemia; this latter disorder is usually associated with a more severe form of hypercholesterolemia, as will be discussed in the next section.

In patients with moderate hypercholesterolemia, an attempt should be made to categorize the type of abnormality before treatment is instituted. If the disorder is hereditary, screening of family members may reveal the etiology. In patients with familial combined hyperlipidemia, a variety of lipoprotein patterns may be found in afflicted family members. In those with familial hypercholesterolemia, family members will generally show elevations of cholesterol, near normal triglycerides, tendon xanthomatosis, and premature atherosclerosis. In polygenic hypercholesterolemia, family members frequently have mild to moderate elevations in plasma cholesterol, but levels are generally not as high as in familial hypercholesterolemia. Also, in work-up of patients with moderate hypercholesterolemia, consideration must be given to the possibility that their elevated cholesterol levels are secondary to another disease such as the nephrotic syndrome, hypothyroidism, obstructive liver disease, or rare dysglobulinemias.

Before treatment of hypercholesterolemia is instituted, at least three blood samples should be obtained to verify the existence of elevated cholesterol and to serve as a baseline for the evaluation of therapy. The primary treatment of moderate hypercholesterolemia should again be dietary alteration. Weight reduction should be instituted if the patient is overweight. Also, animal fats should be excluded from the diet, and polyunsaturated fats should be given in their place. If dietary changes are adhered to vigorously, plasma concentrations of cholesterol will decrease significantly in most patients, and in a few, levels will fall to the range of 200 mg/dl; in these patients drug therapy may not be necessary.

However, in many patients with moderate hypercholesterolemia, adherence to diet is poor, or dietary change is relatively ineffec-

tive, and in these patients consideration must be given to drug therapy. The most effective agents for lowering plasma cholesterol are the bile acid binding resins (cholestyramine, colestipol) (48). When these agents are given in the dose range of 16 to 20 g/day, a lowering in plasma cholesterol of 20 to 30% is frequently attained. The bile acid binding agents retard the reabsorption of bile acids, and thus decrease the rate of return of bile acids to the liver; this change leads to a release of feedback inhibition on the conversion of cholesterol into bile acids by bile acids, an increased degradation of cholesterol into bile acids with a drain on hepatic cholesterol, and finally to a reduction in plasma cholesterol. In general the binding resins are safe and effective drugs; however, because of the large doses required they are somewhat inconvenient and unpleasant to take, and they frequently cause constipation. At present, there is a large national trial being carried out to determine whether cholestyramine therapy can actually retard the development of atherosclerotic disease in patients with hypercholesterolemia, but several years will be required before a final answer is obtained.

Another agent for lowering cholesterol levels is nicotinic acid; when this drug is given in a dose of 3 to 6 g/day, cholesterol levels are usually decreased in the range of 10 to 20% (15). In addition to lowering cholesterol levels, nicotinic acid also decreases triglycerides (49). Available evidence suggests that nicotinic acid lowers cholesterol and triglycerides by blocking the hepatic secretion of lipoproteins (50). Nicotinic acid was one of the agents used in the Coronary Drug Project (CDP) (15); this clinical trial was designed to test whether cholesterol lowering by drugs would prevent the recurrence of myocardial infarction and prolong life in patients who had previously suffered a myocardial infarction. Many of the patients in this study had mild hypercholesterolemia, but few had moderate hypercholesterolemia. In the CDP, nicotinic acid caused a consistent lowering of plasma cholesterol, and it produced a significant decrease in the recurrence of myocardial infarction; however, the drug did not alter the overall mortality rate, as compared to control subjects. Whether the drug would be

effective in reducing both morbidity and mortality in patients with moderate hypercholesterolemia, who have had no previous clinical evidence of atherosclerosis, is yet to be determined. While nicotinic acid appears to be generally safe, the drug nevertheless can cause certain unpleasant side effects such as flushing of the face, gastrointestinal upset, and itching and rashes of the skin.

Another drug which can be used for treatment of moderate hypercholesterolemia is clofibrate (Atromid-S). This drug is most effective for reduction of triglycerides (and VLDL), but it can also lower plasma cholesterol levels in many patients; on the average, cholesterol levels are reduced by 5 to 15% with clofibrate (15). However, the full effect of clofibrate on cholesterol metabolism is not revealed by changes in plasma concentrations; for example, it has been shown that clofibrate causes a significant mobilization of cholesterol from tissue pools even when it does not cause a marked reduction of cholesterol in the plasma (51). Since accumulation of cholesterol in arterial tissues is a major factor in atherosclerosis, it is possible that mobilization of tissue cholesterol could retard or reverse atherogenesis. On the other hand, in the CDP, clofibrate was not effective in either reducing the recurrence of myocardial infarction or decreasing overall mortality (15). Again, however, it remains to be determined whether this drug will alter atherogenesis in subjects without manifest atherosclerotic disease.

Severe hypercholesterolemia

According to our present criteria, sustained cholesterol levels greater than 350 ml/dl constitute severe hypercholesterolemia. In patients with this degree of abnormality, premature atherosclerosis is extremely common (6-8). In severe hypercholesterolemia, dietary factors may play some role, but they are generally much less important than genetic factors. The most common cause of severe hypercholesterolemia appears to be familial hypercholesterolemia (25, 26); less frequently this degree of hypercholesterolemia can be found in patients with familial combined hyperlipidemia or polygenic hypercholesterolemia. Also marked increases in plasma cholesterol can

occur in patients with hypothyroidism and nephrotic syndrome.

Diagnosis of familial hypercholesterolemia should be suspected in patients with marked elevations in plasma cholesterol, tendon xanthomatosis, premature atherosclerotic disease, and a family history of these disorders. The diagnosis is confirmed by finding hypercholesterolemia and tendon xanthomata in relatives.

The primary therapy for patients with familial hypercholesterolemia is again diet, and the diet should be rich in polyunsaturated fats and low in animal fats. However, in most patients dietary change alone is usually not sufficient to bring lipid levels into the normal range, and drug therapy must be considered. The most effective single agent is usually a bile acid binding resin; in most patients with familial hypercholesterolemia, significant reductions in plasma cholesterol can be obtained with this type of drug (48). In patients with severe hypercholesterolemia who do not respond adequately to a single drug, an enhanced reduction may be obtained by use of drugs in combination (52-55).

In those patients who cannot adhere reliably to dietary change or drug treatment, the possibility of an ileal exclusion operation should be entertained. This operation, as described by Buchwald (18, 56), causes a diversion of the lower one-third of the small intestine from the fecal stream. Since bile acids are reabsorbed almost entirely within the ileum, the operation has the same effects as resin therapy. In general the operation is well tolerated except that some patients have persistent diarrhea; in many of these patients, the diarrhea can be controlled with cholestyramine (57). The operation usually allows the patient to be free of dietary and drug treatment, and in the long run it is more economical because of the lack of need for prolonged drug treatment.

In summary, hypercholesterolemia can occur with varying degrees of severity, and it can be induced by many factors—genetics, environmental, and disease processes. If a decision is made to treat elevations in plasma cholesterol levels, consideration must be given to the severity and multiple causes when choosing therapeutic modali-

ties (diets, drugs, or ileal exclusion operation).



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THE UNIVERSITY OF CHICAGO,
THE DIVISION OF THE BIOLOGICAL SCIENCES,
AND THE PRITZER SCHOOL OF MEDICINE,
Chicago, Ill., May 16, 1977.

HON. GEORGE MCGOVERN,
Select Committee on Nutrition and Human Needs,
Washington, D.C.

DEAR SENATOR MCGOVERN: With reference to your letter of May 4, 1977 I am happy to provide an opinion on the potential involvement of the United States Government in nutritional policies for the American people.

I read the booklet "Dietary Goals for the United States" prepared by the Select Committee that you chair and find myself in complete agreement with the list of recommendations contained in pages 65 and 75. I share the view that the public is, in general, poorly informed about nutrition due to disinterest, poor understanding and to incorrect information contained in lay journals or magazines. I strongly feel that a well-sustained federally-financed educational program under the supervision of recognized authorities will lead to an improved knowledge of nutritional matters by the American people. This in turn will promote a better understanding of the benefits that derive from good food habits. I also believe that there is already a good deal of convincing evidence which relates diet to cardiovascular disorders and that such information ought to be appropriately made available to the public at large. I don't feel, however, that at least at this time, significant changes in dietary habits ought to be imposed indiscriminately on all American citizens who ought to retain their right to choose whether they are to commit themselves to a given diet regardless of the recommendations by experts. I must add that even those that today wish to comply with recommendations by physicians or nutritionists, when away from home, experience difficulties in continuing their diets owing to non-availability of special diets in public restaurants or cafeterias currently geared to "healthy" customers. The educational programs ought to precede potential future recommendations for changes in food habits: any successful implementation of dietary regulations will require an educated public who must be able to readily perceive the potential negative aspects of diets that experts now consider as risk factors in terms of cardiovascular diseases.

Sincerely yours,

ANGELO M. SCANU, M.D.,
Professor, Departments of Medicine and Biochemistry.

LYNN COMMUNITY HEALTH & COUNSELING CENTER,
Lynn, Mass., June 13, 1977.

HON. GEORGE MCGOVERN,
The U.S. Senate,
Washington, D.C.

DEAR SIR: I am writing to support the Dietary Goal Recommendations of the Committee on Nutrition and Human Needs. These goals would address some of the nutrition problems that I have identified in the enclosed report. They do not, however, directly address the

crucial problem of the food industry being profit-oriented without responsible nutrition policies being required of it.

I suggest recommendations from U.S.D.A. to industry about:

(1) Ceasing to create markets for artificially-colored and artificially-flavored high-sugar or high-fat foods.

(2) Maintaining an appropriate nutrient per calorie ratio in foods.

I also suggest that the U.S.D.A. start a campaign to encourage the use of fresh fruits and vegetables and whole grains. This is important for nutrition, but industry won't touch it because there is no profit involved.

I hope you can put this information to good use.

Sincerely,

BARBARA YOST, R.D., *Nutritionist*.

Enclosure.

NUTRITION IN LYNN, MASSACHUSETTS—A ONE YEAR STATUS REPORT

I have been a community nutritionist in Lynn, Massachusetts, for a year. Lynn is a town with a large welfare population, high unemployment, and frequent school drop-outs. I work with low-income pregnant women and parents of young children. Many of the parents are interested in "doing better by" their children, but lack the resources—both monetary and educational.

I have approximately 800 food histories (women and children) on file, and feel competent to enumerate some of the nutrition problems of my community. By observation and inference, I suspect that some of these problems are nationwide. These problems are:

(1) *Excessive milk consumption*.—(a) Milk replaces other necessary foods:

(1) 2-3 cups per day or the equivalent is plenty. Many children drink 6-8 cups (about 5 percent drink $\frac{1}{2}$ gallon per day or more).

(2) Milk and dairy products are low in iron and many "milk children" are anemic.

(b) Mother's waste money on milk.

(c) Excessive milk contributes to increased saturated fat in diet, with an increase in blood cholesterol and statistically increased heart disease.

(2) *Frequent sugar exposures*.—(a) The number of sugar exposures largely determines the dental decay that will be caused.

(b) Most sweet foods are empty calories and promote poor food habits which last a lifetime.

(c) Sweet foods seem "addictive" to many children, who often refuse foods that are not sweet.

(d) Mother's, in ignorance and out of economic necessity, give children artificially colored and flavored drinks like kool ade, xarex, etc. which advertise themselves as "fruit drinks" and are sold next to fruit juice in the supermarket. These are not juices—they are sugar, water, coloring and flavoring.

(3) *Frequent use of overly processed foods*.—(a) Overuse of high-salt, high-saturated fat, nitrate-laden processed meats which are possible carcinogenic, have a lower nutrient calorie ratio, and discourage children from learning to chew meats.

(b) Artificially colored and flavored sugar-laden foods like cereals, jellos, drinks, desserts, toppings and spreads have a low nutrient/calorie ratio and no redeeming value except profit to manufacturers. High-salt, high-fat snack foods also have a very low nutrient/calorie ratio. A low nutrient/calorie ratio leads to frequent adult obesity without adequate nutrient intake.

(4) *Very low fiber diets.*—(a) Fiber is probably essential to proper bowel functioning and shortened intestinal transit time.

(b) Cereal fiber carries with it many essential nutrients, the intake of which is low in highly refined diets.

For example: Pantothenic acid; vitamin E; biotin; iron; chromium; magnesium, manganese and so forth.

(5) *Industry irresponsibility.*—Many misconceptions about what to eat and feed to children stem directly from media propaganda, paid for by large “food” industries with no nutrition policy, but many policies about making markets for more junk foods and increasing profits by using the cheapest ingredients, nutritious or not.

(6) *School feeding programs.*—The school feeding program, instead of being an example of good nutrition, is saddled by a tight budget and archaic food standards. Fresh fruits are rare, fresh vegetables are not used except in salads, highly processed foods are emphasized and whole grain products are never used.

(7) *Management of infant feeding.*—(a) Many local doctors do not follow A.M.A. Pediatric and nutritional guidelines for infant feeding and start whole milk, skim milk or solids very early. There is some evidence that early feeding of solids can lead to allergic symptoms like gastro-intestinal upset, rhinitis, asthma.

(b) Little nutrition education is done with young mothers except through the federally sponsored W.I.C. and Children and Youth Medical Programs.

(8) *Pre-natal nutrition.*—(a) Nutrition education is superficially treated by many pre-natal health care providers. This passes up one of the best and most important times to focus on preventative health care.

(b) Overweight pregnant women are encouraged to lose or not gain, weight. Weight gain in pregnancy is important to fetal development and weight reduction can wait until the baby is born.

(c) Little is taught to pregnant women about choosing, preparing and serving food for children.

THE UNIVERSITY OF NEBRASKA MEDICAL CENTER,
Omaha, Nebr., June 17, 1977.

HON. GEORGE S. MCGOVERN,
Senate Office Building,
Washington, D.C.

DEAR SENATOR MCGOVERN: I appreciate having the opportunity to comment on the recent report “Dietary Goals for the United States”, by the Senate Select Committee on Nutrition and Human Needs.

I appreciate the time and effort expended by the committee in the preparation of the report as well as the concern that prompted it as expressed by Dr. D. M. Hegsted on page three of the report, “Ischemic

heart disease, cancer, diabetes and hypertension are the diseases that kill us. They are epidemic in our population. We cannot afford to temporize. We have an obligation to inform the public of the current state of knowledge and to assist the public in making the correct food choices. To do less is to avoid our responsibility”.

Although our present diet is associated with ischemic heart disease, cancer, diabetes and hypertension, it is also associated with the longest life expectancy in history. Life expectancy today is 71.9 years and is rising slowly to a plateau value of between 73 and 74 years. The maximum average life expectancy at birth, in the absence of overt disease, is around 85 years, while the maximum life span of man is approximately 100 years.

The spectrum of diseases that kill us is associated with the average life expectancy; in 1900 when average life expectancy was 47.3 years the leading causes of death were tuberculosis and other infectious diseases. Today, with a life expectancy of 71.9 years, we are beset by cancer and cardiovascular diseases. “Conquest” of cancer would increase average life expectancy by about $2\frac{1}{2}$ years while elimination of cardiovascular disease would increase average life expectancy somewhere in the neighborhood of $7\frac{1}{2}$ years. If we should succeed in significantly reducing deaths from cancer and cardiovascular diseases, other leading causes of death will appear. Most likely these will be diseases of the central nervous system, disorders that will be accompanied by a significant increase in the incidence of senile dementia—already a major problem in our society.

In view of the foregoing I think it is very unlikely that the suggested dietary changes would have a marked influence on the health and well-being of our population. I suspect that increasing carbohydrate consumption and reducing the overall fat, cholesterol, and sugar consumption as specified under dietary goals 1, 2, 4 and 5, would have a slight beneficial effect. Reduction of salt consumption should also have a modest beneficial effect. The decrease in salt intake suggested by dietary goal 6 may be difficult to achieve; probably reduction to 5 grams or so a day would be more realistic.

I am concerned about dietary goal 3. Increasing the amount of polyunsaturated fat in our diet will produce changes in fatty acid composition of cells and tissue throughout the body, including that of the lipoproteins in the blood. These widespread lipid changes may have deleterious effects which outweigh any benefits derived from the associated lower serum cholesterol levels. Increasing the degree of unsaturation of dietary lipid would be expected to be associated with an increased rate of lipid peroxidation both in serum and in the arterial wall, which may in turn contribute to an increased rate of atherogenesis (Harman, D.: *Atherogenesis in Mini-Pigs: Effect of Dietary Fat Unsaturation and of Copper*. *Atherosclerosis: Proceedings of the Second International Symposium*, edited by R. J. Jones, Springer-Verlag, New York, 1970, pp. 472–475). Recent prostaglandin research (Moncada, S., Higgs, E. A., and Vane, J. R.: Human Arterial and Venous Tissues Generate Prostacyclin (Prostoglandin X), a Potent Inhibitor of Platelet Aggregation. *The Lancet*, I, 18–20, 1977) also indicates that increasing the unsaturation of dietary lipids may be associated with an increased incidence of cardiovascular disease. Further, increasing the peroxidizability of dietary

lipids may lead to an increased rate of degeneration of the central nervous system (Harman, D., Hendricks, S., Eddy, D. E., and Seibold, J.: Free Radical Theory of Aging: Effect of Dietary Fat on Central nervous system (Harman, D., Hendricks, S., Eddy, D. E., and Seibold, Eddy, D. E., and Harman, D.: Free Radical Theory of Aging: Effect of Age, Sex and Dietary Precursors on Rat-Brain Docosahexanoic Acid. J. Amer. Geriatric Soc., 25: 220-229, 1977) as well as to a decrease in immune responses (Harman, D., Heidrick, M. L. and Eddy, D. E.: Free Radical Theory of Aging: Effect of Free-Radical-Reaction Inhibitors on the Immune Response. J. Amer. Geriatric Soc., 25— in press—1977). Clearly, more studies with polyunsaturated fats are required before changes in dietary consumption, either up or down, can be advocated.

The suggested dietary goals are directed at our current leading causes of death. It would be better to direct our nutritional goals to the problem that really concerns us. How do we achieve the longest possible, useful, healthy life-span? Can we modify the amount and/or the pattern of food intake and increase the healthy life span as suggested by the early work of McKay? Another nutritional approach, illustrated in attached papers, is based on the possibility that free radical reactions are involved in aging and degenerative diseases. Application of current biomedical aging research knowledge to human nutrition would very likely increase our span of healthy productive life by 5 to 10 to 15 years.

I concur with the five recommendations presented in the report by the Senate Select Committee except that in recommendation 1, I would rewrite the first sentence to read, "That Congress provide money for public education programs in nutrition".

I agree with your statement in the foreword to the committee report that the nutritional habits of the American people are a major health concern. Future increases in the span of healthy life are most apt to come from changes in our diet. To this end the Senate Select Committee on Nutrition and Human Needs can play a significant role.

Cordially,

DENHAM HARMAN, M.D., Ph.D.,

Millard Professor of Medicine, Professor of Biochemistry, Executive Director, American Aging Association.

Enclosure.

ATHEROGENESIS IN MINIPIGS: EFFECT OF DIETARY FAT UNSATURATION AND OF COPPER*

(By Denham Harman)

Atherogenesis is enhanced by substances capable of irritating the arterial wall [613]. A possible constant source of irritative compounds may be the reaction of molecular oxygen with serum and arterial wall lipids [611]. The readily oxidized polyunsaturates comprise about 30 percent of the total fatty acids, present mainly as esters, in the lipids of both serum [1158] and atherosclerotic plaques [225]. Hence, the oxidation products, including peroxides and compounds

*Atherosclerosis: Proceedings of the Second International Symposium. Edited by Richard J. Jones. Springer-Verlag, New York 1970.

of higher molecular weight formed through oxidative-polymerization, as well as substances arising from the reaction of the intermediate lipid free radicals with proteins and other substances, may be produced in amounts large enough to make a significant contribution to atherogenesis. The foregoing suggests that the long-term ingestion of increased amounts of polyunsaturates, increasing the unsaturation of serum and tissue lipids, might actually enhance atherosclerosis [611, 612] even though they tend to lower serum cholesterol levels [656, 791].

In an attempt to evaluate the possibility that lipid peroxidation is significantly involved in atherogenesis, two experiments have been carried out with uncastrated male pigs. Pigs were employed for this study, for under normal living conditions they spontaneously develop atherosclerotic lesions which are very similar, both grossly and microscopically, to those of humans [527, 895, 1030, 1601]. On the assumption that the morphologic similarity of the lesions in swine and man is a result of similar pathogenic processes, the pig should be a good animal for evaluating factors presumed to be involved in human atherogenesis. In the first experiment pigs were fed diets containing 30 percent by weight of either lard or safflower oil while in the second, pigs were given diets containing 15 percent by weight of either lard or safflower to which was added 0.0, 0.05, or 0.10 percent by weight of cupric acetate, a good catalyst for the reaction of molecular oxygen with organic compounds [1487].

METHODS

Genetically small male uncastrated pigs, "Nebraska Miniature Swine" [1534], were ear marked and then allocated at random to form groups of 10 pigs each. Each group was placed in a concrete block pig house (10 × 10 ft) with an outside run (10 × 16 ft); both areas have concrete floors. The pigs were weighed and bled (superior vena cava) at intervals of about six months. The serum samples were analyzed for total cholesterol [854, 1334].

The aortas, removed with the first part of their major branches, except for the coronary arteries in the first experiment, were stained with Sudan IV [698] and graded for atherosclerosis on a scale of 0-4+, [405, 825]; in the second experiment, the coronary arteries were also graded. Grading was done blind by three individuals on two occasions one week apart and the average of the six gradings for each area determined. In grading, no distinction was made between fatty and fibrous lesions.

Autopsy serum samples were analyzed for cholesterol and phospholipids (2nd Experiment).

First Experiment. The two groups of pigs were started at age of about three months, shortly after being placed in the pens, on one of the following diets: Group 1—Basal diet (70 percent w, i.e., by weight) + antioxidant free lard (30 percent w); Group 2—Basal diet + safflower oil (30 percent w).

The base diet was a high protein, high vitamin diet such that with the addition of the 30 percent w fat the final diet was considered to be nutritionally satisfactory for young, rapidly growing pigs. The final diet contained 13.8 percent w protein, 31.0 percent w lipid, 11.5

percent fiber, 6.0 percent w ash, 8.4 mg of vitamin E per pound (not counting that present in the added lipid) and 516 mg choline per pound; the final diets contained 1,530 cal/pound, 83.0 percent of the calories from lipid.

The diets were prepared weekly and kept stored in a cool area prior to use; the pigs were fed once a day from a common food trough in each pen. The edible grade safflower¹ oil was shipped in drums and was reported to be stable; i.e., peroxide value below 1.0 mg/kg, for the approximately six-week period required to utilize the contents of a drum. The lard was antioxidant free.

At age 24 months, having been on the special diets for 21 months, the pigs (fasting) were electrocuted, exsanguinated, and complete autopsies performed.

Second Experiment. Six groups were started at age five months on the following diets: (1) Basal diet (85 percent w) + antioxidant free lard (15 percent w); (2) Diet 1 plus 0.05 percent w cupric acetate; (3) Diet 1 plus 0.10 percent w cupric acetate; (4) Basal diet (85 percent w) + safflower oil (15 percent w); (5) Diet 4 plus 0.05 percent w cupric acetate; and (6) Diet 4 plus 0.10 percent w cupric acetate.

TABLE.—PIG ATHEROGENESIS

Experiment number and diet	Serum			Atherosclerosis ¹		
	Weight (pounds)	Cholesterol (mg/100 ml)	Phospholipid (mg/100 ml)	Aorta		Coronary art.
				Arch	Abd.	
EXPERIMENT 1						
30%w/Lard..... ²	312.5±71.7	76.4±14.3	-----	0.34±0.32	0.40±0.42	-----
30%w/Safflower oil.....	261.1±51.9	85.5±18.4	-----	.24±.26	.65±.81	-----
EXPERIMENT 2						
15%w/Lard+0.00%w/Cu ⁴	200.5±35.2	113.5±15.2	126.8±25.6	.33±.23	.37±.29	0.48±0.32
15%w/Lard+0.05%w/Cu.....	213.0±33.6	102.3±36.1	127.6±24.2	.46±.54	.44±.51	.63±.70
15%w/Lard+0.10%w/Cu.....	216.3±28.3	101.3±17.1	119.1±15.4	.32±.24	.37±.40	.39±.15
15%w/Safflower oil+0.00% Cu.....	202.5±55.8	85.0±14.0	88.7±23.8	.21±.20	.35±.29	.39±.20
15%w/Safflower oil+0.05% Cu.....	214.4±21.0	88.7±11.0	92.2±16.2	.22±.18	.19±.24	.11±.18
15%w/Safflower oil+0.10% Cu.....	211.8±44.0	69.5±7.6	74.3±12.8	.38±.43	.41±.53	.42±.15

¹ Atherosclerosis graded on basis of 0-4+; 0 indicating no atherosclerosis and 4 involvement of the entire intimal surface by atherosclerotic lesions.

² Mean ± standard deviation.

³ The three average serum cholesterol values obtained for the safflower oil groups during life were all lower than those for the lard group; there is no explanation as to why the autopsy average serum cholesterol value for the safflower oil group is higher than for the lard group.

⁴ Cu=Cupric acetate.

Cupric acetate powder was mixed in diets (2), (3), (5) and (6) just prior to feeding. The diets contained 16.4 percent w protein, 16.3 percent w lipid, 13.9 percent w fiber and 7.3 percent w ash; 800 mg choline, 7 mg of copper and vitamin E (25 mg plus that present in the added lipid) per pound. In the final diet, 56.7 percent of the total calories were derived from fat. The animals were fed an average of 2.5 pounds of food per day per pig.

After 21 months on the diets, at age 26 months, the animals were killed and autopsied as in Experiment 1.

¹ We wish to thank the Pacific Vegetable Oil Corporation, Richmond, Calif., for the safflower oil used in this study.

RESULTS

Autopsy data for Experiments 1 and 2 are given in the Table.

In Experiment 1, six of the ten pigs in the safflower oil group were found to have multiple hard yellowish masses, ranging in size from a few millimeters to 10 cm in diameter, embedded in the omental and peritoneal fat; these masses were composed of varying amounts of adipose tissue, fat-like droplets, giant cells, cellular debris and collagenous tissue. The kidney of a pig receiving safflower oil had significant tubular dilation and interstitial fibrosis associated with a few inflammatory cells while a second pig in the group had a slight degree of kidney fibrosis.

In Experiment 2 the incidence of the yellowish abdominal masses in the pigs on safflower oil was about 30 percent. The average size and number were markedly decreased, and there were no kidney lesions.

Aortic atherosclerosis in both experiments was small and variable, averaging about 0.3 in the arch and around 0.4 in the abdominal aortic area. Although some trends can be discerned in comparing the various atherosclerosis gradings in the two experiments, the differences are not statistically significant.

DISCUSSION

Feeding male uncastrated minipigs for 21 months on diets expected to result in differing rates of peroxidation of serum and vessel wall lipids did not produce statistically significant differences in aortic and coronary artery atherosclerosis. Some trends were seen which may be real. In both experiments the aortic arch atherosclerosis tended to parallel the serum cholesterol levels, being lower with the safflower oil diets as compared to lard. In contrast, abdominal aortic and coronary artery atherosclerosis was about the same in the pigs on either the lard or safflower oil diets. Addition of cupric acetate tended to enhance both aortic and coronary artery atherosclerosis; the effect appeared somewhat greater with the safflower oil diets. The results with cupric acetate support the possibility that the elevated levels of serum copper found in employed males with a history of myocardial infarction [614] were also present prior to infarction.

Thus the data are compatible with the possibility that lipid peroxidation contributes to atherogenesis, the enhancement being partially or completely nullified by the lowered serum cholesterol levels produced by the dietary alterations. Further, lipid peroxidation may be involved in regulation of serum lipid levels; for dietary copper, like polyunsaturates, tended to lower both serum cholesterol and phospholipid concentrations.

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HUMAN ARTERIAL AND VENOUS TISSUES GENERATE PROSTACYCLIN (PROSTAGLANDIN X), A POTENT INHIBITOR OF PLATELET AGGREGATION

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SUMMARY

Fresh rings of arteries and veins obtained from surgical specimens generated an unstable substance, prostacyclin (prostaglandin X,

[P.G.X]) which is a potent inhibitor of platelet aggregation. The spontaneous generation of prostacyclin as well as its generation from exogenous arachidonic acid was inhibited by incubation of the tissues with a prostaglandin-synthetase inhibitor such as indomethacin, whilst the generation induced by prostaglandin endoperoxides was not. 15-Hydroperoxyarachidonic acid (a lipid hydroperoxide) inhibited the generation of prostacyclin in all three situations. It is postulated that prostacyclin is important for prevention of deposition of platelets on the vessel wall and that the inhibition or prevention of the generation of prostacyclin is important in the genesis of diseases, especially those in which increased lipid peroxidation occurs, such as atherosclerosis.

INTRODUCTION

Prostaglandin endoperoxides (P.G.G₂ and P.G.H₂), thromboxane A₂ (T.X.A₂), or a mixture of both (rabbit-aorta-contracting substance [R.C.S.] [1] can be generated by guineapig perfused lungs [1], by chopped rabbit spleen [2], by various microsomal preparations [3-7], and by bloodplatelets [8-10]. One biological activity of prostaglandin endoperoxides is to induce platelet aggregation [10] and at least part of this activity is due to their conversion into the more potent and more unstable T.X.A₂ [11].

We have described a novel metabolic transformation of prostaglandin endoperoxides into another unstable substance which we called postaglandin X (P.G.X) [12]. The structure has now been elucidated [13] and the substance renamed prostacyclin (see fig. 1). Prostacyclin produced by vessel walls of pig and rabbit [12, 14-16] causes vasodilatation and inhibits platelets aggregation [12]. In this last respect prostacyclin is the most potent endogenous substance so far described.

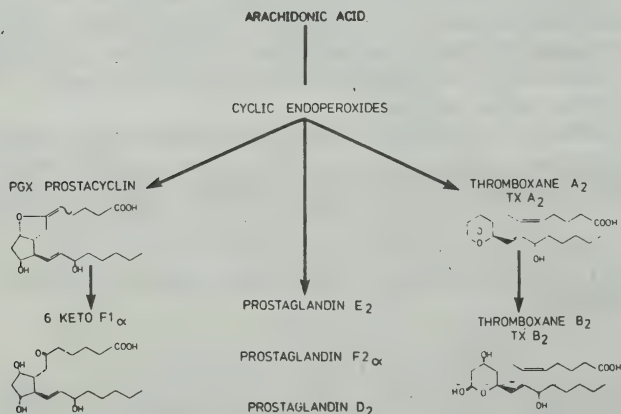


FIGURE 1.—Metabolism of arachidonic acid showing structures of prostacyclin, T.X.A₂, and their stable derivatives.

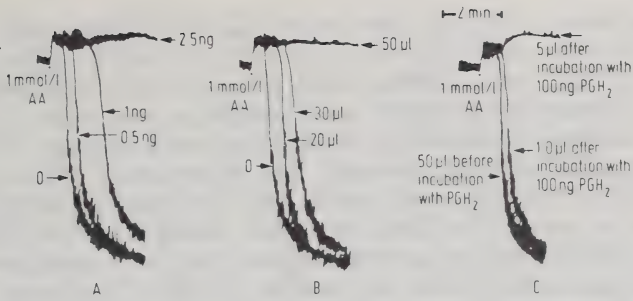


FIGURE 2

(A) Inhibition of platelet aggregation by prostacyclin: p.g.X (prepared as described in Methods) in concentrations (per ml) of 0.5, 1.0, or 2.5 ng incubated for 1 min in P.R.P. produced dose-dependent inhibition of aggregation induced by arachidonic acid (AA) (1 mmol/l).

(B) Inhibition of platelet aggregation by prostacyclin generated from rings of human vascular tissue: Cut rings (59 mg) were incubated in 200 µl of tris buffer (0.05 mol/l, pH 7.5) for 3 min at 22°C. Samples of 20, 30, and 50 µl of the supernatant from the incubation mixture, incubated for 1 min in P.R.P. produced a volume-dependent inhibition of the aggregation induced by arachidonic acid (1 mmol/l).

(C) Generation of anti-aggregatory activity from postaglandin endoperoxide (P.G.H₂) by rings of human vascular tissue: The rings were washed several times in tris buffer until 50 µl of supernatant from a 3 min incubation in 200 µl tris buffer at 22°C produced no antiaggregatory activity. When the rings were then incubated for 3 min at 22°C in 200 µl tris buffer containing 100 ng p.g.H₂ volumes of 1.0 and 5.0 µl from the supernatant inhibited the aggregation caused by 1 mmol/l arachidonic acid.

We have postulated an interaction between platelets and vessel wall [12, 14–16] by which endoperoxide released in the vicinity of the vessel wall by platelets is enzymically converted to prostacyclin, which then actively prevents platelet deposition. Our finding that a lipid peroxide, 15-hydroperoxyarachidonic acid (15-H.P.A.A.), inhibits the production of prostacyclin *in vitro*, [14, 15] has led us to suggest that inhibition of this enzyme by lipid peroxides could contribute to those diseases in which excessive lipid peroxidation occurs, such as atherosclerosis.

We have now shown that human vascular tissue also generates prostacyclin.

MATERIALS AND METHODS

Blood from healthy volunteers who had not taken aspirin for at least 15 days was withdrawn from the antecubital vein and placed in a plastic container with 3.15 percent (w/v) sodium citrate (nine volumes of blood to one of citrate). Platelet-rich plasma (P.R.P.) was then obtained by centrifuging the blood at 200 *g* for 15 min. Platelet aggregation was studied in 1 ml samples *in vitro* in a double-channel Payton aggregometer. Aggregation was initiated with sodium arachidonate (0.3–1.6 mmol/l).

Human colic or gastric arteries or veins (100–200 mg wet weight and approximately 1.5–3 mm in diameter) were removed from fresh

surgical specimens, cut into fine rings (0.5–1 mg) and kept in "tris" buffer (0.05 mol/l, pH 7.5) at 0°C for no more than 3 h after removal. Rings (35–60 mg) were incubated in 200 μ l of same tris buffer for 3 min at 22°C. Samples (1–100 μ l) of the supernatant were added to the P.R.P. 1 min before the addition of sodium arachidonate. When antiaggregatory activity was detected, the supernatant was allowed to stand at 37°C for 10 min, or it was boiled (0.25 min) and its effect on aggregation retested. The tissue was then washed several times with tris buffer (200 μ l) until no antiaggregatory activity could be detected in a 50 μ l aliquot after 3 min incubation at 22°C. The tissue was then incubated with sodium arachidonate (0.2–20 μ g in 200 μ l) or P.G.G₂ or P.G.H₂ (100 ng in 200 μ l) for 3 min at 22°C and the antiaggregatory activity of the solution was assessed. The amount of antiaggregatory activity produced by incubation of the tissue in tris buffer alone or with sodium arachidonate or prostaglandin endoperoxide was compared with the antiaggregatory activity produced by standard prostacyclin obtained by incubating P.G.H₂ with pig aortic microsomes as previously described. [12]

In other experiments, pieces of tissue (15–30 mg) were placed in the P.R.P. itself and stirred at 37°C for 3–10 min before testing the effect of addition of arachidonate to the P.R.P. The results were compared with those obtained when the tissue was pretreated with 15-H.P.A.A. (10–20 μ g/ml) for 5 min at 22°C before incubation with the P.R.P.

RESULTS

Generation of Prostacyclin by Arterial and Venous Rings.—Vascular rings (35–60 mg wet weight) incubated for 3 min at room temperature released prostacyclin. Venous rings produced more (0.8 ± 0.6 ng/mg, four experiments) than arterial rings (0.11 ± 0.02 ng/mg, eight experiments). This release occurred in the first 3 min of incubation. After washing the tissue, further incubations yielded less prostacyclin. In fact, in every experiment the amount produced decreased progressively after each washing until no activity could be detected (3–5 washings). Incubation of arterial or venous tissue for 5 min in buffer containing indomethacin (5 μ g/ml) or 15-H.P.A.A. (20 μ g/ml) blocked this basal release.

After three to five washings, when antiaggregatory activity could no longer be detected, arachidonate (1–100 μ g/ml) was added. 3 min later, formation of prostacyclin was determined. The conversion rate of arachidonate was low in both arteries and veins, usually below the limits of detection (0.01 percent). However, in three arterial samples there was 1.3 ± 1 percent conversion and in one vein 0.6 percent (mean of two observations). This conversion was inhibited by pretreatment of the tissue with indomethacin (5 μ g/ml) or 15-H.P.A.A. (10–20 μ g/ml). When the rings were incubated with P.G.H₂ high conversion was observed both with arteries (75 ± 13 percent, six experiments) and veins (68 ± 18 percent, three experiments). Fig. 2 shows one of these experiments. This conversion was prevented by pretreatment with 15-H.P.A.A. (20 μ g/ml) but not by pretreatment with indomethacin (5 μ g/ml). The basal as well as the stimulated antiaggregatory material released was destroyed by boiling the sample for 15 sec or by incubating at 37°C for 10 min (fig. 3).

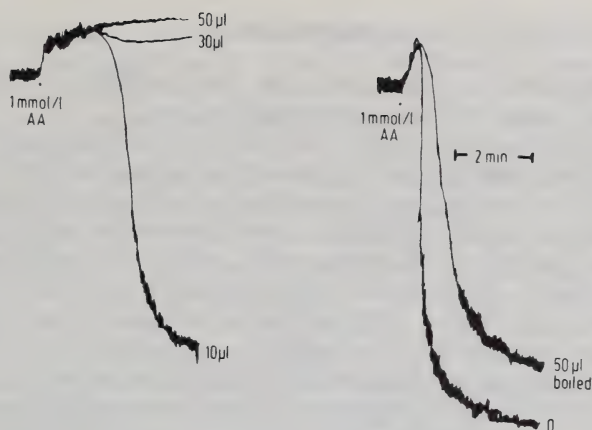


FIGURE 3.—Effect of boiling on antiaggregatory activity produced by rings of human vascular tissue.

50 μ l of the supernatant of the incubation mixture of cut vascular rings (35–60 mg) in 200 μ l tris (3 min, 22°C) completely inhibited the aggregation caused by 1 mmol/l arachidonic acid. When this supernatant was boiled for 15 sec a 50 μ l sample had a much reduced inhibitory effect on platelet aggregation.

Addition of vascular rings to the P.R.P.—Rings of arteries (15–30 mg) added to the P.R.P. and incubated for 3–10 min before addition of arachidonate prevented platelet aggregation. The amount of antiaggregatory activity generated depended directly on the weight of tissue added and also on the time of incubation with the P.R.P. Tissues which showed little or no basal release of prostacyclin sometimes caused aggregation when added to the P.R.P. When other rings were incubated with 15-H.P.A.A. (10–20 μ g/ml) for 5 min at 22°C before their addition to the P.R.P., there was no antiaggregatory activity, and sometimes aggregation was induced (fig. 4).

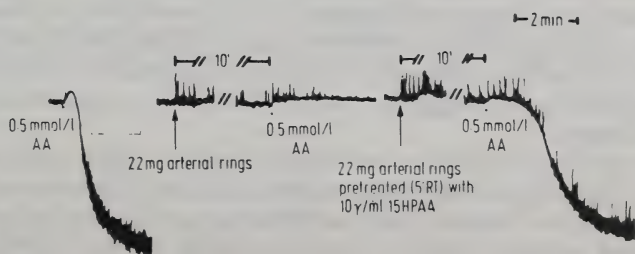


FIGURE 4.—Inhibition of platelet aggregation by rings of human vascular tissue.

Cut rings (15–30 mg), when incubated at 37°C in human P.R.P. for 10 min, inhibited the aggregation produced by 0.5 mmol/l arachidonic acid. When the rings were pretreated by incubation with 15-H.P.A.A. (20 μ g/ml) for 5 min at 22°C, and then added to the P.R.P., aggregation was once more observed after addition of 0.5 mmol/l arachidonic acid.

DISCUSSION

The present results show that our observations in pig [12] and rabbit [14, 15] vascular tissue also apply to man.

The presence of an enzyme in the vascular wall which synthesises a powerful antiaggregating substance explains the long recognised fact that platelets do not adhere to normal vascular endothelium. [17] Contrary to being inert to platelets, vessels possess an active mechanism based on the formation of prostacyclin which defends them against platelet deposition. Heyns et al. using human tissue, found an antiaggregatory activity in the arterial wall, associated with the intima. Although they attributed this activity to degradation of adenosine diphosphate, it now appears more likely that it was due to prostacyclin formation. Association of prostacyclin synthetase with the endothelial cells would explain why the initiation of a mural thrombus, particularly in the arterial tree, is associated with endothelial damage. Not only are the platelets exposed to the subendothelial layers, in which proaggregating material is present (especially collagen [17]), but also there would be a decrease (at the local site) of prostacyclin formation. However, prostacyclin formation by adjacent undamaged endothelium would limit the growth of the thrombus to the damaged area.

Human vessels show a very low conversion-rate of arachidonate into prostacyclin (0.01 percent or less). The fact that this is much lower than the conversion of 0.5–1 percent observed in rings of rabbit coeliac and mesenteric arteries could be due to the different arteries used. In rabbits, we used the main artery trunks (coeliac and mesenteric) whereas in human, the third or fourth level branching of the main arteries was used. It might also be due to a species difference. However, both species were effective in converting prostaglandin endoperoxides into prostacyclin. Moreover, when rings of arteries were added to the platelet-rich plasma, antiaggregating activity was generated according to the amount of tissue added and the incubation time. These facts support our hypothesis that the vessel wall is fed by endoperoxides synthesised by platelets in active contact with the endothelial layer, giving rise to a platelet-vessel wall interaction essential to the homeostatic functioning of the vascular tree.

Some rings which did not produce much prostacyclin or had been treated with 15-H.P.A.A. actually induced aggregation. Lack of prostacyclin unmasks the proaggregatory activity of subendothelial structures like collagen.

Human veins have a higher endothelial content than arteries, which may explain their apparently higher basal release of prostacyclin. This, together with other factors such as differences in rheological characteristics, could account for the fact that veins do not develop atherosclerosis.

The inhibition by 15-H.P.A.A. of the enzyme in human tissue which produces prostacyclin occurs at concentrations which are also effective in inhibiting this enzyme in other species [14, 15] Lipid peroxidation has been implicated in conditions such as carcinogenesis, ageing, and atherosclerosis; certainly atherosclerotic plaques contain increased amounts of lipid peroxides. Thus, inhibition of prostacyclin synthesis by lipid peroxides could be the biochemical basis for the increased tendency to thromboembolic complications during atherosclerosis.

Aspirin-like drugs inhibit the second phase of platelet aggregation and increase bleeding time in vivo. Consequently, these drugs have been tested in clinical trials for the prevention of thrombosis. The fact that the results have not been dramatic may be linked with the site of action of aspirin-like drugs. They inhibit endoperoxide production (see fig. 1) so that formation of prostacyclin is inhibited, as is that of TxA_2 . Clearly, drugs which selectively inhibit TxA_2 formation would be theoretically preferable as antithrombotic drugs since generation of prostacyclin would remain unimpaired. Antioxidants such as vitamin E have been used empirically with controversial success in the treatment of obstructive vascular diseases and coronary artery disease. Inhibition of lipid peroxidation by antioxidants could, by protecting prostacyclin synthetase, be the basis for long-term administration in the prevention of atherosclerosis or other diseases in which excessive lipid peroxidation has been suspected.

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Free Radical Theory of Aging: Effect of Age, Sex and Dietary Precursors on Rat-Brain Docosahexanoic Acid*

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ABSTRACT: Increasing the peroxidizability of dietary fat has an adverse effect on the function of the central nervous system (CNS) in the rat. This effect may be influenced by the level of docosahexanoic acid, a highly unsaturated fatty acid, selectively concentrated in the phospholipids of brain membranes. This study was aimed at determining the influence of age, sex, and the nature of a dietary lipid supplement — linolenic acid (18:3 ω 3), docosahexanoic acid (22:6 ω 3), or the same amount of 22:6 ω 3 in the form of menhaden oil triglycerides — on the rate of increase in the percentage of 22:6 ω 3 in the whole-brain fatty acids of rats between the ages of 1 and 12 months. The dietary lipid supplements were reflected in linear increases in the brain 22:6 ω 3 of female rats throughout the study. Between 6 and 12 months of age, the rate of incorporation of dietary 22:6 ω 3 and its precursors into the brain 22:6 ω 3 of male rats dropped. At 12 months it was about half that for females in the case of 22:6 ω 3 and menhaden oil, and about zero for 18:3 ω 3. It is suggested that dietary 22:6 ω 3 and its precursors may modify CNS function by altering membrane function and peroxidizability through changes in the concentration of 22:6 ω 3 in membrane phospholipids.

Rat performance in maze and discrimination learning situations is impaired as the peroxidizability of dietary fat is increased (1). This effect of dietary fat may be produced, at least in part, by enhancing the level of more-or-less random free radical reactions throughout the brain. The enhancement is brought about through increases in the peroxidizability of the dietary fat or through the provision of easily oxidized lipids or their precursors that are concentrated in brain tissues, thereby enhancing the susceptibility of the tissues to free radical reactions.

The major contributor to the possible latter mode of brain dysfunction may be the ω 3 family of fatty acids, the group of polyunsaturated fatty acids whose first double bond, starting from the CH₃ end, is between carbons 3 and 4. Both lino-

lenic acid (carbon number 18:3 ω 3) and docosahexanoic acid (22:6 ω 3) are avidly taken up from the diet (2-4) and reflected in increased brain levels of 22:6 ω 3. Brain 22:6 ω 3 is tenaciously retained, resulting in increased levels with increasing age, largely at the expense of 22:5 ω 6 (2).

Brain 22:6 ω 3 is concentrated in the phospholipids of neurons, both in the perikaryon and the synaptic area (5-8); the percentages of 22:6 ω 3 in the acyl chains of the phosphatidylethanolamine, phosphatidylserine plus phosphatidylinositol, and phosphatidylcholine fraction are about 20-30, 10-15 and 1-3 respectively. Retinal rods are also rich in 22:6 ω 3 (9). Presumably the presence of this highly unsaturated, readily peroxidized, fatty acid in phospholipids has a beneficial effect on membrane permeability to water and organic compounds (10) and on the activities of membrane-bound enzymes (11).

The minimal dietary requirements, if any, for 22:6 ω 3 or its precursors (mainly 18:3 ω 3) for satisfactory central nervous system (CNS) function, has not been determined because of difficulties in

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eliminating 18:3 ω 3 from the diet (3). It is also not known if there is a value or a range of values of brain 22:6 ω 3 associated with optimal brain function.

The purpose of the present study was to determine the influence of age, sex, and the nature of the dietary lipid supplement — 18:3 ω 3, 22:6 ω 3 or distilled triglycerides of menhaden oil — on the rate of increase in the percentage of 22:6 ω 3 in the fatty acids of whole-brain lipid.

METHODS AND RESULTS

The 130 rats used in this study were the seventh generation offspring born in this laboratory of Sprague-Dawley rats obtained (Charles River Breeding Laboratories, Wilmington, MA) at weaning in October 1972. The rats were maintained in an air-conditioned room at 75–78°F at a humidity of 50–60 percent. They were kept, 4 to a cage (stainless steel, 11.5 × 18.5 × 6.5 inches). Cages were changed two or three times per week; the bedding was sterilized shredded corn cobs (Sani-i-Cel, Paxton Processing Co., Paxton, IL). Food and water were provided ad libitum. The 23 dams were given a semisynthetic diet (12) containing 5%w (by weight) of edible grade safflower-olive (oleinate, a mutant of safflower oil in which oleic acid replaces linoleic acid) (Pacific Vegetable Oil Corp., Richmond, CA) and 20 mg of α -tocopherol acetate per 100 grams of finished diet; at 115 days of age, and thereafter, unesterified α -tocopherol was used instead of the acetate. When the rats were 117 days old, 1 male, same age as the females and given prior to mating the same diet, was placed in a cage with 4 females for a period of 7 days and then removed. The offspring (seventh generation) were culled to 8 per litter at 6 days of age. At 23 days of age the 130 rats (67 females and 63 males) were weaned, sexed and caged 4 per cage.

At age 26 days the offspring were divided into three approximately equal groups as shown in Table 1.

The rats of *Group I* were divided into 4 dietary subgroups: 1) control diet; 2) control plus 50 mg of 18:3 ω 3 (Nu Chek Prep, Inc., Elysian, MN); 3) control plus 50 mg of 22:6 ω 3 (90 percent grade, Nu Chek Prep, Inc.); or 4) control plus 377 mg of distilled triglycerides of menhaden oil (kindly supplied by Dr. Neva L. Karrick of the Northwest Fisheries Center, U. S. Dept. of Commerce, Seattle, WA), per 100 grams of finished diet. The fatty acid analyses of the four finished diets are

listed in Table 2. The base diet was prepared every ten to fourteen days and the supplemented diets every six to seven days; the diets were kept in a deep-freeze before use. The rats were fed fresh food daily. Two male and 2 female members of *Group I* were killed by decapitation on days 0, 15 and 30, and like numbers of rats from each of the supplemented groups were killed after days 10, 20 and 30 of the study.

Group II rats were given the control diet until age 147 days, and *Group III* rats until age 391 days, before being divided into the 4 dietary subgroups. The decapitation schedule for the supplemented subgroups of *Group II* and *III* was the same as for *Group I*; the numbers of rats for analysis were also the same except that only 1 male was available in the 18:3 ω 3 subgroup of *Group III*. In the control subgroup of *Group II*, 2 male and 2 female rats were killed at the beginning and at the end of the 30-day supplemented period whereas only 1 male and 2 females were available for the control subgroup of *Group III*; these were killed at the start of the 30-day supplemented period.

After decapitation, whole brains (1.0–1.9 grams, depending upon the age of the rats) were taken immediately, frozen on dry ice, wrapped in aluminum foil and stored in nitrogen-filled vials at –70°C, until the lipid analyses could be carried out. The procedures for brain lipid extraction, conversion of the fatty acid moieties to methyl esters, and analysis of fatty acid composition by gas chromatography have been described previously (2).

The mean \pm the standard error of the mean for the major brain fatty acids for the 4 dietary subgroups for the three supplemented periods are shown in Table 3. The male and female data for *Groups I* and *II*, diets supplemented for 30 days starting at age 27 and 147 days respectively, are combined in the table, as they were essentially the same. Individual male and female rat brain data are shown for *Group III*—diets supplemented for 30 days starting at age 391 days, along with the averages of the combined data. The data of Table 3 for total brain 22:5 ω 6 and 22:6 ω 3, are presented graphically in Figure 1, A and B. The changes in the percentage of 22:4 ω 6, 22:5 ω 6 and 22:6 ω 3 in total brain lipids of rats on the base diet are shown in Figure 2 as a function of age from 26 to 391 days.

The differences between the percentages of a given fatty acid at the end of the 30-day supplemented dietary fat period and at the start for each of the given dietary subgroups, for each of

TABLE 1

Effect of Age, Sex, and Dietary Fat on Fatty Acid Composition of Total-Brain Lipids in Sprague-Dawley Rats. (Supplemental Lipid Feeding Periods and Autopsy Schedule)

Group	Age (days)	Dietary Fat Supplement*			
		None	18:3ω3	22:6ω3	Men- haden Oil
		Autopsy Schedule			
1-48 rats	26	2M†,2F‡			
	36		2M,2F	2M,2F	2M,2F
	41	2M,2F			
	46		2M,2F	2M,2F	2M,2F
2-44 rats	56	2M,2F	2M,2F	2M,2F	2M,2F
	147	2M,2F			
	157		2M,2F	2M,2F	2M,2F
	167		2M,2F	2M,2F	2M,2F
3-38 rats	177	2M,2F	2M,2F	2M,2F	2M,2F
	391	1M,2F			
	401		1M,2F	2M,2F	2M,2F
	411		2M,2F	2M,2F	2M,2F
	421		2M,2F	2M,2F	2M,2F

* At 26, 147 and 391 days of age, groups of rats that had been receiving base diet were subdivided into 4 dietary groups by adding either nothing (control), 50 mg of 18:3 ω 3, 50 mg of 22:6 ω 3, or 377 mg of distilled triglycerides of menhaden oil to the diet.

† Male.

‡ Female.

the three supplemented periods, are shown in Table 4. Changes in 22:6 ω 3 are shown in Figure 3.

DISCUSSION

The percentage of 22:6 ω 3 in the total-brain lipid of rats receiving the base diet rose steadily, almost linearly for females and somewhat less so for males, throughout the course of this study — from age 26 days to age 391 days. The increases in brain 22:6 ω 3 with age are due to the small amount (about 0.1 percent) of 18:3 ω 3 present in the safflower-olive (oleinate) in the base diet. The increases in brain 22:6 ω 3 were roughly paralleled by the decreases in 22:5 ω 6.

Increases in dietary 18:3 ω 3, 22:6 ω 3 or distilled triglycerides of menhaden oil were reflected in virtually linear increases in the percentage of brain 22:6 ω 3 during the three age periods studied, viz, 26-56, 147-177 and 391-421 days. The increases for the age period 26-56 days were nearly the same when the diet was supplemented with either 50 mg of 22:6 ω 3 per 100 grams of diet or 377 mg of distilled triglycerides of menhaden oil (containing 50 mg of 22:6 ω 3 in ester form) — 8.1 per cent and 10.6 per cent respectively. The increase produced by adding 50 mg of 18:3 ω 3 to

100 grams of the base diet was about half, i.e., 3.9 per cent. The increase in brain 22:6 ω 3 resulting from administration of the three lipid supplements during the second age period, 147-177 days, was roughly half that observed for the first age period. During the third age period, 391-421 days, the percentage increase of 22:6 ω 3 in brain total lipid was the same as for the second age period for all three lipid supplements for females, but about half for males receiving 22:6 ω 3 or menhaden oil and practically zero for males receiving 18:3 ω 3.

Previous work (2) indicated that the level of 22:6 ω 3 in total brain lipid would increase little after 6 months of age; therefore the present experiment was programmed for one year. This impression was in error. Instead, at 12 months of age, the female rat continues to convert dietary 18:3 ω 3 and 22:6 ω 3 (the latter either as the free acid or in glyceride form) into brain 22:6 ω 3 at the same steady linear rate as observed at 147-177 days of age. This ability is significantly impaired in males, particularly for 18:3 ω 3.

The maximum percentage of 22:6 ω 3 in the total brain lipid of male and female rats that can be achieved by dietary manipulation, is not known. In this study the highest brain 22:6 ω 3 level, 13.1

TABLE 2
Fatty Acid Composition of the Diets

Carbon Number	Diet			
	Base*	18:3 ω 3**	22:6 ω 3†	Menhaden Oil‡
10	0.10	0.14	0.21	—
12	—	—	—	0.22
14	0.20	0.23	0.23	1.16
15§	0.01	0.02	0.02	0.08
16	5.79	5.43	5.36	8.20
16:1 ω 7	—	—	—	0.57
17:1§	—	—	—	0.13
18	0.67	0.44	0.75	0.67
18:1 ω 9	71.43	70.78	69.38	61.66
18:2 ω 6	19.74	19.29	19.70	20.61
20	—	—	0.12	0.23
18:3 ω 3	0.10	2.47	0.13	0.08
20:1 ω 7	0.18	0.10	0.17	0.86
20:2§	1.56	1.04	0.24	0.44
20:4 ω 6	—	—	—	0.13
20:5 ω 3	—	—	—	2.31
22:1	—	—	—	0.43
22:6 ω 3	—	—	3.65	1.68

* Semisynthetic diet containing, as sole source of lipid, 5%w of oleinate and 20 mg of α -tocopherol per 100 grams of finished diet.

** 50 mg of 18:3 ω 3 added per 100 grams of base diet.

† 50 mg of 22:6 ω 3 (90% grade) added per 100 grams of base diet.

‡ 377 mg of distilled triglycerides of menhaden oil (equivalent to 50 mg of 22:6 ω 3) added per 100 grams of base diet.

§ Tentative identification.

May 1977

EFFECT OF AGE, SEX AND DIET ON RAT-BRAIN LIPIDS

TABLE 3
Effect of Age, Sex, and Dietary Fat on Fatty Acid Composition of Total Brain Lipids in Sprague-Dawley Rats

A. Group I: Control diet supplemented with 18:3ω3, 22:6ω3 or menhaden oil, from 27 to 46 days of age									
Control Diet (CD)					CD + 18:3ω3				
Carbon Number	Age, Days				Age, Days				
	26	41	56		36	46	56		
16	20.6 ± 0.4	18.5 ± 0.2	18.3 ± 0.1		19.7 ± 0.2	18.7 ± 0.3	18.2 ± 0.1		
18	18.9 ± 0.2	19.7 ± 0.4	19.8 ± 0.1		20.0 ± 0.2	20.4 ± 0.2	20.7 ± 0.3		
18:1ω9	20.0 ± 0.6	21.7 ± 0.5	22.6 ± 0.4		21.4 ± 0.2	22.2 ± 0.4	21.9 ± 0.3		
20:4ω6	15.0 ± 0.1	13.2 ± 0.1	12.2 ± 0.7		13.4 ± 0.3	12.7 ± 0.1	12.2 ± 0.1		
22:4ω6	4.5 ± 0.1	4.2 ± 0.1	4.3 ± 0.1		4.1 ± 0.1	3.8 ± 0.2	3.9 ± 0.1		
22:5ω6	14.6 ± 0.2	14.4 ± 0.4	14.0 ± 0.3		13.7 ± 0.2	11.8 ± 0.1	10.8 ± 0.4		
22:6ω3	2.1 ± 0.2	2.0 ± 0.1	2.3 ± 0.0		3.2 ± 0.1	4.5 ± 0.1	6.0 ± 0.2		
CD + Menhaden Oil									
Carbon Number	Age, Days				Age, Days				
	36	46	56		36	46	56		
16	19.3 ± 0.1	18.4 ± 0.2	17.9 ± 0.1		18.9 ± 0.2	18.7 ± 0.2	17.9 ± 0.1		
18	20.0 ± 0.3	20.6 ± 0.2	20.2 ± 0.1		19.7 ± 0.2	20.2 ± 0.1	20.7 ± 0.2		
18:1ω9	20.3 ± 0.1	22.0 ± 0.4	22.5 ± 0.3		21.4 ± 0.4	22.3 ± 0.3	23.0 ± 0.4		
20:4ω6	13.2 ± 0.1	12.0 ± 0.2	11.8 ± 0.1		13.0 ± 0.2	12.1 ± 0.2	11.4 ± 0.2		
22:4ω6	4.1 ± 0.2	3.6 ± 0.1	3.3 ± 0.2		3.7 ± 0.1	3.5 ± 0.1	3.6 ± 0.4		
22:5ω6	13.1 ± 0.1	10.1 ± 0.4	8.4 ± 0.2		11.1 ± 0.2	7.4 ± 0.1	5.4 ± 0.1		
22:6ω3	4.8 ± 0.2	7.6 ± 0.3	10.1 ± 0.3		6.7 ± 0.3	10.8 ± 0.4	12.7 ± 0.1		
B. Group II: Control diet supplemented with 18:3ω3, 22:6ω3 or distilled triglycerides of menhaden oil, from 147 to 177 days of age									
Control Diet (CD)					CD + 18:3ω3				
Carbon Number	Age, Days				Age, Days				
	147	167	177		157	167	177		
16	18.2 ± 0.3		17.0 ± 0.2		17.4 ± 0.2	17.1 ± 0.3	17.4 ± 0.2		
18	18.8 ± 0.1		19.5 ± 0.6		19.8 ± 0.5	19.8 ± 0.7	18.8 ± 0.3		
18:1ω9	26.2 ± 0.3		27.9 ± 0.3		27.0 ± 0.4	27.0 ± 0.1	28.0 ± 0.2		
20:4ω6	12.8 ± 0.3		12.1 ± 0.1		11.8 ± 0.0	12.0 ± 0.1	12.1 ± 0.2		
22:4ω6	3.7 ± 0.1		3.6 ± 0.1		3.4 ± 0.1	3.5 ± 0.1	3.4 ± 0.2		
22:5ω6	13.3 ± 0.1		10.8 ± 0.5		10.7 ± 0.3	10.3 ± 0.3	10.1 ± 0.3		
22:6ω3	3.9 ± 0.4		4.4 ± 0.5		3.8 ± 0.3	5.2 ± 0.4	6.2 ± 0.3		

TABLE 3—Continued

B. Group II: Control diet supplemented with 18:3 ω 3, 22:6 ω 3 or distilled triglycerides of menhaden oil, from 147 to 177 days of age (Continued)

Carbon Number	CD + 22:6 ω 3			CD + Menhaden Oil		
	Age, Days			Age, Days		
	157	167	177	157	167	177
16	17.3 \pm 0.2	17.5 \pm 0.1	17.1 \pm 0.3	17.3 \pm 0.2	17.3 \pm 0.2	17.1 \pm 0.2
18	20.1 \pm 0.9	18.7 \pm 0.3	18.3 \pm 0.2	19.1 \pm 0.2	20.7 \pm 0.4	19.5 \pm 0.2
18:1 ω 9	26.6 \pm 0.7	27.6 \pm 0.2	27.7 \pm 0.4	27.2 \pm 0.2	26.5 \pm 0.3	27.7 \pm 0.1
20:4 ω 6	11.8 \pm 0.2	12.2 \pm 0.2	11.7 \pm 0.2	12.3 \pm 0.1	11.6 \pm 0.2	11.6 \pm 0.3
22:4 ω 6	3.3 \pm 0.2	3.3 \pm 0.2	3.2 \pm 0.1	3.8 \pm 0.2	3.8 \pm 0.2	3.2 \pm 0.0
22:5 ω 6	11.1 \pm 0.6	9.8 \pm 0.3	8.8 \pm 0.2	10.3 \pm 0.2	8.1 \pm 0.1	6.8 \pm 0.4
22:6 ω 3	4.5 \pm 0.3	6.5 \pm 0.4	8.1 \pm 0.4	5.2 \pm 0.4	6.8 \pm 0.4	8.8 \pm 0.4

C. Group III: Control diet supplemented with 18:3 ω 3, 22:6 ω 3 or distilled triglycerides of menhaden oil, from 391 to 421 days of age

Carbon Number	Control Diet (CD)			CD + 18:3 ω 3		
	391 Days of Age			401 Days of Age		
	Female	Male	Avg. \pm s.e.m.	Female	Male	Avg. \pm s.e.m.
16	17.3	17.2	17.1 \pm 0.2	16.6	16.5	16.9 \pm 0.3
18	19.8	19.4	19.7 \pm 0.1	19.6	20.4	19.7 \pm 0.4
18:1 ω 9	27.8	27.9	28.1 \pm 0.2	28.2	27.9	28.3 \pm 0.3
20:4 ω 6	11.3	11.7	11.6 \pm 0.2	11.6	10.8	11.4 \pm 0.3
22:4 ω 6	3.0	3.2	3.2 \pm 0.1	3.2	3.0	3.3 \pm 0.2
22:5 ω 6	9.6	8.2	9.0 \pm 0.4	7.4	9.5	8.8 \pm 0.7
22:6 ω 3	7.0	8.1	7.0 \pm 0.6	8.6	7.8	7.6 \pm 0.7

Carbon Number	CD + 18:3 ω 3			CD + 18:3 ω 3		
	411 Days of Age			421 Days of Age		
	Female	Male	Avg. \pm s.e.m.	Female	Male	Avg. \pm s.e.m.
16	16.5	16.1	16.5 \pm 0.2	17.2	15.4	16.6 \pm 0.5
18	19.4	20.1	19.4 \pm 0.1	19.4	19.5	19.3 \pm 0.1
18:1 ω 9	28.2	28.8	28.2 \pm 0.2	28.7	28.8	29.0 \pm 0.2
20:4 ω 6	11.3	11.1	11.5 \pm 0.2	10.9	11.3	11.5 \pm 0.3
22:4 ω 6	3.2	2.8	3.3 \pm 0.2	2.9	3.2	3.2 \pm 0.1
22:5 ω 6	7.1	8.3	8.5 \pm 0.3	7.8	6.6	8.2 \pm 0.7
22:6 ω 3	9.8	9.1	7.9 \pm 0.9	9.2	10.4	7.9 \pm 1.1

TABLE 3—Continued

C. Group III: Control diet supplemented with 18:3ω3, 22:6ω3 or distilled triglycerides of menhaden oil, from 391 to 421 days of age
CD + 22:6ω3

Carbon Number	401 Days of Age				411 Days of Age				421 Days of Age			
	Female	Male	Avg. ± s.e.m.	Female	Male	Avg. ± s.e.m.	Female	Male	Avg. ± s.e.m.	Female	Male	Avg. ± s.e.m.
16	16.6	16.4	17.1	16.7	16.7	16.7 ± 0.2	16.7	17.0	16.8 ± 0.1	17.1	15.8	16.7 ± 0.3
18	19.6	19.4	19.4	19.9	19.6	19.4 ± 0.2	19.6	19.1	19.7 ± 0.3	19.4	19.5	19.6 ± 0.1
18:1ω9	28.6	28.9	28.8	29.3	28.2	28.9 ± 0.1	28.2	28.3	28.8 ± 0.4	28.1	28.6	28.8 ± 0.3
20:4ω6	11.4	11.3	11.9	11.7	11.5	11.6 ± 0.1	11.5	11.6	11.4 ± 0.1	11.1	11.2	11.3 ± 0.1
22:4ω6	3.3	3.0	3.6	3.5	3.2	3.4 ± 0.1	3.2	3.3	3.2 ± 0.1	3.3	3.3	3.3 ± 0.1
22:5ω6	8.9	8.3	8.7	9.1	8.8	8.8 ± 0.2	8.8	7.5	7.5 ± 0.3	5.7	6.6	6.7 ± 0.4
22:6ω3	8.5	9.3	6.5	5.8	7.5	7.5 ± 0.8	10.3	9.3	8.7 ± 0.7	11.7	11.2	9.8 ± 0.9
CD + Menhaden Oil												
Carbon Number	401 Days of Age				411 Days of Age				421 Days of Age			
	Female	Male	Avg. ± s.e.m.	Female	Male	Avg. ± s.e.m.	Female	Male	Avg. ± s.e.m.	Female	Male	Avg. ± s.e.m.
16	16.1	16.9	17.0	16.5	16.6	16.6 ± 0.2	16.6	16.7	16.6 ± 0.0	16.1	17.2	16.8 ± 0.3
18	19.4	20.0	18.4	20.0	18.9	18.3 ± 0.4	18.9	18.3	19.9 ± 0.2	19.2	19.9	19.2 ± 0.3
18:1ω9	30.7	28.3	29.5	28.8	29.3	29.3 ± 0.5	28.4	28.8	29.1 ± 0.4	28.2	29.7	28.2 ± 0.7
20:4ω6	10.8	11.3	12.2	11.9	11.5	11.6 ± 0.3	11.5	11.6	11.5 ± 0.2	11.3	12.4	11.6 ± 0.3
22:4ω6	3.0	3.1	3.4	3.3	3.2	3.2 ± 0.1	3.1	3.2	3.3 ± 0.1	3.3	3.2	3.1 ± 0.1
22:5ω6	7.6	8.5	8.6	8.8	8.4	8.4 ± 0.3	6.6	6.4	6.8 ± 0.2	5.1	7.3	6.8 ± 0.6
22:6ω3	9.2	8.6	6.5	6.7	7.7	7.7 ± 0.7	10.7	11.4	9.3 ± 1.0	13.1	11.5	10.6 ± 1.1

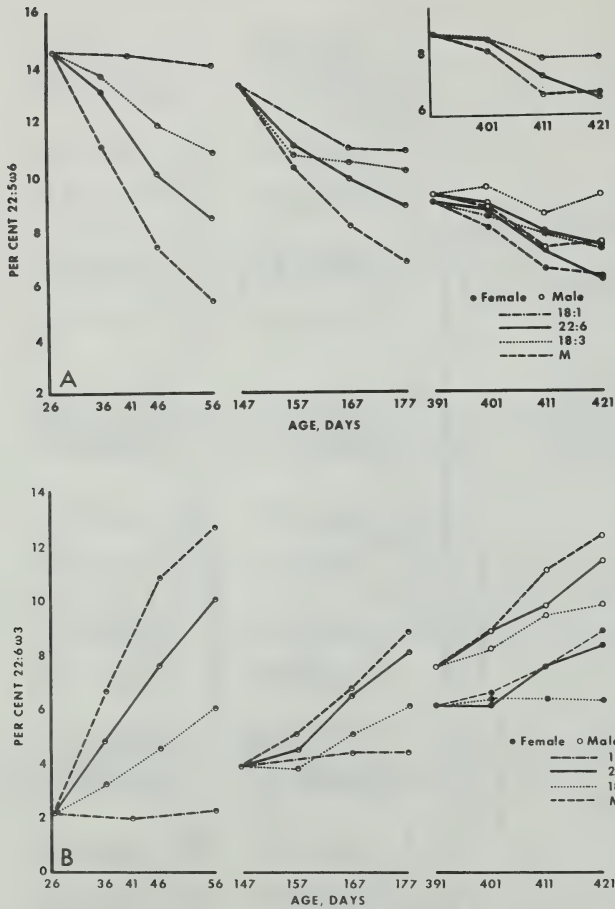


Fig. 1. Effect of age, sex and dietary fat on: A. The percentage of 22:5ω6 in the fatty acids of whole-brain lipid. B. The percentage of 22:6ω3 in the fatty acids of whole-brain lipid. (Sprague-Dawley rats.)

per cent of total fatty acids, was observed for a female rat given menhaden oil supplement for 30 days starting at age 391 days; the corresponding value for males from the same menhaden oil group was 9.7. It is also not known if neuronal populations differ in fatty acid composition and ability to concentrate 22:6ω3, nor if the composition of the components of the synaptic areas mirror corresponding elements of the perikaryon.

The fact that 22:6ω3 is selectively concentrated

in brain phospholipids suggests that it has a beneficial effect on membrane function, probably on permeability and membrane-bound enzymes. Hence the findings of the present study imply that variations in CNS function between individuals may be partially a reflection of the variables influencing brain 22:6ω3 levels, viz, age, sex and dietary precursors. This suggestion is supported by the recent observation (13) that the performance of rats in a discrimination learning situa-

tion was correlated positively with the level of 22:6 ω 3 in brain phosphatidylethanolamine and phosphatidylserine-phosphatidylinositol. Brain 22:6 ω 3 levels were altered by feeding semisynthetic diets containing safflower oil, corn oil or soybean oil as the sole source of lipid.

It would be anticipated that as the percentage of 22:6 ω 3 in total brain lipid increased, lipid peroxidation would increase (even though dietary vitamin E was more than sufficient to prevent overt vitamin E deficiency) and at some point might result in clinically significant behavioral

changes. These changes would not necessarily be accompanied by decrements in other body tissues because of the lesser tendency of 22:6 ω 3 to concentrate in them. Thus, enhanced lipid peroxidation in the synaptic areas, which are rich in polyunsaturated fatty acids, might contribute to deleterious alterations in behavior in a manner similar to that caused by β -hydroxydopamine (14) or by the anesthetic, halothane (15, 16). Support for this possibility comes from studies of neuritic plaques (senile plaques). The plaques, present in the cortex and basal ganglia of normal

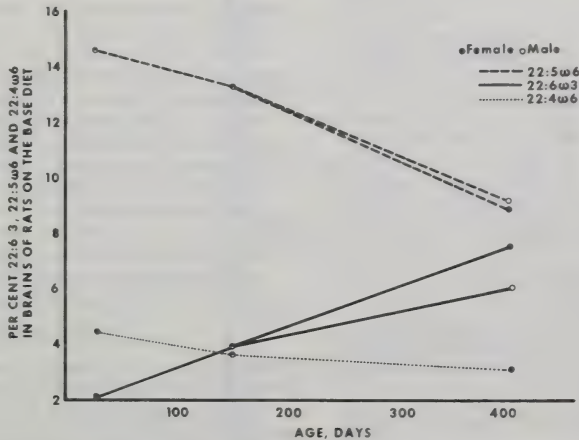


Fig. 2. Effect of age on the percentage of 22:4 ω 6, 22:5 ω 6, and 22:6 ω 3 in the fatty acids of whole-brain lipid of rats receiving the base diet.

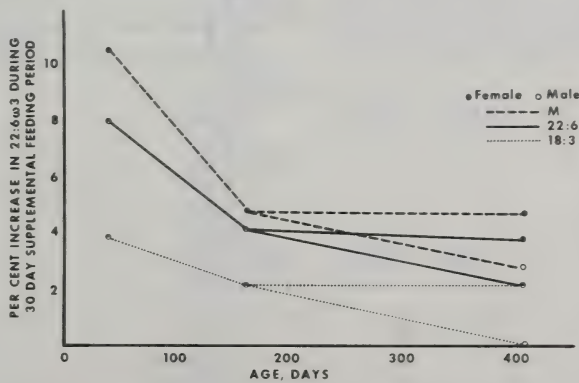


Fig. 3. Effect of age, sex and dietary fat on the percentage increase in 22:6 ω 3 in the fatty acids of whole-brain lipid during each of the three 30-day supplemented feeding periods.

TABLE 4
Effect of Age and Sex on Changes in Whole-Brain Fatty Acid Composition Produced by Supplementing the Diet for 30 Days with Either 18:3, 22:6 or Menhaden Oil (Sprague-Dawley)

Age (days)	Diet	Percent Change in Fatty Acid Composition											
		18:0	18:1	18:1 ω 6	Carbon Number 20:4 ω 6			22:4 ω 6	22:5 ω 6	22:6 ω 3			
27-56	Base	2.35		0.80	2.61		-2.87		-0.24		-0.60		0.19
	"	-2.59	+ 18.3*	1.68	1.92		-2.78		-0.62		-3.75		3.93
	"	-2.71	+ 22.6	1.22	2.51		-3.13		-1.19		-6.20		8.06
147-177	Base	2.77	+ Month	1.70	2.96		-3.53		-0.94		-9.18		10.60
	"	1.21		0.71	1.77		-0.68		-0.11		-2.50		0.52
	"	0.76	+ 18.3	0.03	1.90		-0.61		-0.33		-3.21		2.25
391-421	Base	1.04	+ 22.6	0.01	1.51		-1.05		-0.27		-4.15		4.15
	"	-1.05	+ Month	0.65	0.52		-1.12		-0.54		-6.55		4.85
	"												
391-421	Base**	0.13	+ 18.3	-0.70	0.87		-0.15		-0.41		-0.01		-0.06
	"	0.04	+ 22.6	-0.17	0.78		-0.54		-0.39		-1.89		2.07
	"	-0.22	+ Month	1.02	0.41		-0.50		-0.27		-1.79		2.77
391-421	Base**	0.13		-0.70	0.87		-0.15		-0.41		-0.01		-0.06
	"	0.04	+ 18.3	-0.17	0.78		-0.54		-0.39		-1.89		2.07
	"	-0.22	+ Month	1.02	0.41		-0.50		-0.27		-1.79		2.77

* The base diet was supplemented with either 50 mg of linolenic acid (18:3 ω 6), docosahexanoic acid (22:6 ω 3) or 377 mg of distilled triglycerides of menhaden oil, containing 50 mg of 22:6 ω 3 as the triglyceride.

** Data available only for rats aged 391 days.

† Male.

‡ Female.

old people (17), are increased in senile persons (18). The first changes seen in the development of the plaques are alterations in the mitochondria of the axon terminals (19). These mitochondrial changes may be due to peroxidation, for the mitochondria have both a high degree of lipid unsaturation and a high rate of oxygen utilization. The foregoing may be the basis for the observation that rats receiving a semisynthetic diet containing distilled triglycerides of menhaden oil performed more poorly in a Hebb-Williams maze than had been anticipated from mortality data (1).

The present study also suggests that variability in the period of senility prior to death in humans may be due, at least in part, to the differences in brain 22:6 ω 3 attributable to sex and variation in the amount and kind of brain 22:6 ω 3 dietary precursors consumed throughout life. Further, it would be anticipated that variable degrees of dysfunction might occur throughout the CNS with time because of local differences in factors, other than lipid, which influence lipid peroxidation. Among these factors are the rate of oxygen utilization, the concentration of α -tocopherol, and the concentration of peroxidation catalysts such as copper and iron (20).

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Free Radical Theory of Aging: Effect of Dietary Fat on Central Nervous System Function*

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ABSTRACT: Free radical reactions have been implicated in aging. A rise in the level of random free radical reactions in a biologic system might have a greater effect on the central nervous system (CNS) than elsewhere, partly because of the presence of glial cells and the unique connections between neurons. To evaluate this possibility, some animal experiments were conducted. The initial experiment involved old male Sprague-Dawley rats fed (since shortly after weaning) with semisynthetic diets characterized by fat differing in amount or degree of unsaturation. The number of errors made in a Hebb-Williams maze was determined and found to be higher as the amount or degree of unsaturation of the fat was increased. Likewise rats aged 6 and 9 months, fed semisynthetic diets containing 20 percent by weight of lard, oleifate, or safflower oil + α -tocopherol performed significantly better in a discrimination learning situation (Skinner box) than did rats fed a diet containing 20 percent by weight of safflower oil. The diets employed in these studies did not have a significant effect on the mortality rates. These results are compatible with the possibility that enhancing the level of lipid peroxidation has an adverse effect on the CNS, out of proportion to the effect on the body as a whole, as measured by the mortality rate.

Chronic organic brain syndrome (COBS) is a major health problem (1, 2). In this disease the central nervous system (CNS), at least that part involved in higher functions, can be regarded as aging faster than the body as a whole, becoming "old" to the point where the individual is deprived of intellectual and emotional life for a significant period before death. The incidence of COBS rises rapidly with advancing age, beginning at about age 70 (1). Since the median age of the 65+ group is increasing (3), marked

increases can be expected in the number of persons with COBS.

COBS patients can be divided into three large groups on the basis of the major brain lesions: a) senile plaques 47 percent; b) vascular disease 30 percent; and c) mixed "a" and "b" 23 percent (4). Recent work indicates that degenerative changes in aging dendrites (5) may also be involved in COBS.

The etiology of COBS is unknown. Free radical reactions may be involved in the pathogenesis. This class of chemical reaction (6, 7), ubiquitous in biologic systems (8, 9), has been implicated in the degradation of such systems. On this basis, one possible means of decreasing the rate of degradation in the central nervous system and elsewhere, would be to decrease the ingestion of dietary components that might reasonably be expected to participate significantly in more-or-less random free radical reactions in vivo. Fat is such a dietary factor (10), and it is a major component of most human diets. The fatty-acid moieties present in dietary fat differ markedly,

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in the ease with which they are peroxidized (11), i.e., react with molecular oxygen; peroxidation of a polyunsaturated fatty acid such as linolenic acid proceeds much more rapidly than that of stearic acid, a saturated fatty acid. Thus, decreasing the amount or degree of unsaturation of dietary fat might be expected to result in a decreased rate of biologic degradation.

In general, dietary fat might be expected to have an effect on the CNS similar to that on the body as a whole. However, the CNS response may be greater than elsewhere in the organism because the neurons are fixed postmitotic cells with unique connections with other neurons (12), while exchange with the capillaries, in contrast with parenchymal cells elsewhere, is modified by the presence of glial cells. The foregoing characteristics could conceivably make the CNS more susceptible than the rest of the body to accumulative deleterious changes which in turn could be reflected in CNS degradation becoming clinically evident for varying periods before death, the duration of disability being different for each individual.

To evaluate this possibility—that increases in the level of more-or-less random free radical reactions secondary to increased lipid peroxidation might have a selective adverse effect on the CNS—two experiments were conducted in which the relative efficiency in a learning situation was used as a measure of CNS deterioration. In the first study the effect of the amount or degree of unsaturation of dietary fat on the mortality rate for rats was determined, as well as the maze-learning abilities of the animals when old. The second experiment was designed to assess the influence of dietary fats and of one antioxidant, vitamin E, on the learning behavior of relatively young rats, aged 3, 6 and 9 months; operative behavior was evaluated using a discrimination learning paradigm.

EXPERIMENT 1

Method

Four hundred Sprague-Dawley male rats were obtained from Charles River Breeding Laboratories, Wilmington, Massachusetts shortly after weaning and caged, 4 per cage (stainless steel, $11\frac{1}{2} \times 18\frac{1}{4} \times 6\frac{1}{2}$ inches). The rats were maintained in an air-conditioned room at 76–78°F at a humidity of 50–60 percent. Cages were cleaned 2–3 times per week. The bedding consisted of sterilized shredded corn cobs (San-i-Cel, Paxton

Processing Company, Paxton, Illinois). At age 2 months the rats were divided at random into groups and given semisynthetic diets (13) containing 5, 10 or 20%w (percent by weight) of lard, olive oil, corn oil, safflower oil or distilled triglycerides of menhaden oil (Technological Laboratory, Bureau of Commercial Fisheries, Fish and Wildlife Service, U. S. Department of the Interior, Seattle, Washington). There were 28 rats in each of the 5 percent and 10 percent groups and 24 rats in each of the 20 percent groups. The lard (antioxidant-free), olive oil, corn oil and safflower oil were all edible grade, marketed for human consumption.

The composition of the 5%w lipid diet has been published (14); 10 and 20%w lipid diets were prepared at the expense of glucose monohydrate. These diets meet the nutritional requirements of rats (15). Although the amount and type of dietary fat are the only significant variables in these diets, they are not the only variables. Thus, the thiamine requirement of a diet increases with the percentage of carbohydrate. α -Tocopherol acetate was added in the proportion of 20 mg per 100 gm of finished diet, to obviate the possibility of vitamin-E deficiency.

The 5%w, 10%w and 20%w fat diets contained 408, 433 and 483 calories, respectively, per 100 gm. The diets were fed isocalorically; for each gram of diet fed the 20 percent groups, the 10 percent groups received 1.12 gm, and the 5 percent group 1.19 gm. Food consumption was determined once a month for a period of one week; the average amount of food eaten per rat per day in the dietary groups eating the least during the week period was fed to all the groups during the ensuing month. Despite the foregoing, the body weights tended to increase with the level of dietary fat. Judging from the animals' appetites, all the diets were about equally palatable.

The diets were made up once a week and stored in glass jars prior to use; the safflower and menhaden oil diets were kept in a deep-freeze, while the other diets were stored in a cold-room at refrigerator temperature. Samples of the diets were analyzed several times for peroxides by the iodimetric method (AOCS Official Method Cd 8-53), but no peroxides were found.

The rats, ear-coded, were weighed and counted each month. No adjustments were made when deaths decreased the number (originally 4) in a cage.

Learning behavior was assessed at age 32–35 months, with use of an adaptation (16) of the Hebbs-Williams closed field maze (17). In this

maze the positions of the start and goal boxes remain constant while the pathway to the goal box is determined by the positions of adjustable barriers. The field is divided into 36 alternate black and white 5-inch squares. Entrances to any squares which were not in the direct path between the start and goal boxes were counted as errors. The rats were tested under 23-hour food deprivation; reinforcement was accomplished with 45-mg Noyes pellets (P. J. Noyes Co., Lancaster, New Hampshire). The maze floor was covered by a $\frac{5}{8}$ -inch layer of water which served as an additional motivating factor. This supplementary aversive stimulus was found to be necessary for the elicitation of maze-running behavior in these old rats. The animals were given 8 trials in each specific maze configuration. Six practice mazes were run by each rat, to adapt him to the apparatus and handling and to establish the habit of eating in the goal box. The rats were habituated to the test situation between 29 and 31 months of age. Testing in the maze occurred between 32 and 35 months of age.

Results

The percentage surviving, and average weight for each of the 15 dietary fat groups are shown in Table 1 as a function of age in months. The

amount or degree of unsaturation did not have a significant effect on the mortality rate (13). However, the mortality rates for the 20 percent groups were somewhat higher than those for the corresponding 5 percent and 10 percent groups. The mortality rates for the 20 percent groups tended to increase, except for the menhaden oil rats, with increasing unsaturation of the dietary fat. The mortality rates for the menhaden oil groups were lower than had been expected from the degree of unsaturation of the oil; this same effect was also noted in studies at the same time with C3H and Swiss mice (13). The unexpectedly relatively low mortality rates for the menhaden oil groups possibly may have been a result of the less ready enzymatic hydrolysis of the 20:5 and 22:6 fatty acids present in menhaden oil (18) (so that the lipid actually absorbed from the intestinal tract may have been more saturated than that ingested), and of a preferential utilization of highly unsaturated fatty acids for energy production (19).

The maze data are presented in Table 2. The maze study was conducted at a time when the mortality rates for the 15 dietary groups were high, so many rats did not live to complete all the mazes. For this reason the data are divided into three parts; the top third of the table show data for rats that completed mazes 1-4, the

TABLE 1
Effect of Dietary Fat on Mortality Rate (Sprague-Dawley Male Rats)

Effect of Dietary Fat on Mortality Rate (Average Dietary Fat Ratio)											
Fat in Diet, % by Weight	Age of Rats (mos.)	Lard		Olive Oil		Corn Oil		Safflower Oil		Menhaden Oil	
		W ¹	S ²	W	S	W	S	W	S	W	S
5% w groups		N = 28 ³		N = 28		N = 28		N = 28		N = 28	
	28	625	71.4	633	64.3	613	64.3	633	67.9	644	57.4
	30	566	50.0	600	50.0	556	60.7	569	46.4	664	39.3
	32	512	42.9	557	35.7	535	53.6	535	42.9	550	28.6
	34	508	21.4	508	25.0	510	35.7	479	39.3	509	21.4
	36	515	14.3	502	14.3	497	21.4	467	21.4	522	10.7
	38	650	3.6	—	0.0	590	7.2	518	14.3	373	3.6
10% w groups		N = 28		N = 29		N = 28		N = 28		N = 28	
	28	610	53.6	581	72.4	634	60.7	612	64.3	664	67.9
	30	602	32.1	606	55.2	636	53.5	612	50.0	614	57.1
	32	541	28.6	545	44.8	607	39.3	551	39.3	582	50.0
	34	543	17.9	549	31.0	550	32.1	614	39.3	561	39.3
	36	556	3.6	544	13.8	475	17.9	581	17.9	574	10.7
	38	—	0.0	554	3.5	599	3.6	540	7.2	—	0.0
20% w groups		N = 24		N = 24		N = 23		N = 24		N = 24	
	28	662	70.8	704	58.3	762	47.8	678	29.2	679	62.5
	30	626	45.8	659	37.5	689	13.0	731	12.5	718	54.2
	32	612	33.7	575	25.0	646	10.5	668	12.5	638	29.2
	34	582	25.0	546	12.5	574	10.5	561	12.5	673	20.8
	36	504	12.5	—	0.0	715	5.3	662	4.2	735	12.5
	38	532	4.2	—	0.0	—	0.0	—	0.0	540	4.2

¹ = Weight in grams.

² = Percentage of original group still alive.

³ = Initial number of rats.

TABLE 2

Effect of Dietary Fat on Average Number of Errors in a Modified Version of the Hebb-Williams Closed-Field Intelligence Test (Sprague-Dawley Male Rats)

% Fat (by Weight) in Diet	Dietary Fat				
	Lard	Olive	Corn	Safflower	Menhaden
<i>Mazes 1-4: (Age 32-33 months)</i>					
5%w	17.8±5.2 ¹ [12]	20.1±5.6 [10]	23.2±8.4 [13]	21.8±6.4 [11]	25.5±9.8 [7]
10%w	19.5±7.2 [6]	20.6±6.0 [11]	22.6±6.3 [10]	22.9±6.4 [9]	23.1±7.9 [12]
20%w	21.3±6.6 [8]	21.3±6.5 [6]	17.5±7.0 [2]	22.3±7.2 [3]	24.2±5.7 [5]
<i>Mazes 1-8: (Age 32-34 months)</i>					
5%w	17.0±6.6 [7]	19.5±4.6 [5]	21.8±7.1 [10]	20.0±7.2 [9]	24.8±10.3 [5]
10%w	17.9±7.3 [6]	21.0±6.0 [7]	21.1±7.6 [8]	22.1±7.7 [6]	24.3±7.5 [9]
20%w	21.3±6.5 [7]	19.5±7.2 [3]	19.4±7.0 [2]	23.7±8.0 [2]	23.6±5.3 [3]
<i>Mazes 1-12: (Age 32-35 months)</i>					
5%w	18.6±7.1 [5]	21.8±6.0 [4]	22.9±7.0 [7]	19.1±7.3 [6]	26.7±10.3 [4]
10%w	20.5±9.8 [4]	24.9±8.7 [6]	24.1±8.8 [6]	25.0±7.4 [4]	25.8±7.4 [8]
20%w	22.0±7.8 [5]	21.7±6.9 [2]	24.8±8.2 [1]	28.4±10.4 [2]	27.0±7.5 [3]

¹ = Standard deviation.

² = Number of rats.

middle third for those finishing mazes 1-8, and the bottom third for those completing all 12 of the standardized mazes. Each figure in the table is the average number of errors per maze ± the standard deviation made by each rat completing the maze series; thus, each of the 12 rats in the 5%w lard group that completed mazes 1-4 made an average of 17.8 ± 5.2 errors (i.e. the total number of errors made in running a given maze 8 times) for each of the four mazes.

In general the number of maze errors increased both with an increase in the amount of dietary fat and an increase in unsaturation of the dietary fat. Statistical analysis (variance) of the data for the animals that completed all 12 mazes—combining the data of the 10 percent and 20 percent groups because of the small number of rats in the latter—showed that this conclusion was valid at $P < 0.05$.

EXPERIMENT 2

Six-Month-Old Rats

Method

Male and female Sprague-Dawley rats were obtained at weaning and caged and maintained as in the initial study. At the age of 1 month the females were given semisynthetic diets (13) containing either 5 or 20%w (percent by weight) of lard, oleinate, safflower oil, or safflower oil plus 20 mg of α -tocopherol acetate per 100 gm of finished diet; the lipids were of edible grade. The fatty acid composition of the three dietary lipids is shown in Table 3. When the rats were 3 months old, one male of the same age as the females and

TABLE 3
Dietary Lipids: Fatty Acid Analysis

Carbon Number	Safflower (%)	Lard ^a (%)	Safflower-Olive (%)
10			0.1 ^a ±0.1 ^c
12			0.2±0.1
14	0.5 ^a ±0.3 ^c	1.7 ^a ±0.1 ^c	0.4±0.3
16	6.7±0.6	26.5±0.2	5.8±0.6
16:1 ω 7		2.1±0.4	0.1±0.05
18	1.6±0.3	12.1±0.7	1.2±0.1
18:1 ω 9	11.1±0.05	49.8±1.7	75.5±0
18:2 ω 6	79.7±0.1	10.3±0.2	15.8±0.9
20 or 22 acids	0.1±0.05	2.4±1.4	

^a The average of two samples taken at a 6-month interval from the dietary oil.

^b The average of three samples taken at intervals within a year.

^c Standard error of the mean.

^d The lard contained a trace amount of 22:6 ω 3 as the free acid.

fed prior to mating on a commercial pelleted diet (Rockland, Teklad, Inc., Monmouth, Ill.), was placed in a cage with 4 females for a period of 7 days and then removed. The offspring at 23 days of age, were weaned, sexed, caged 4 per cage, and maintained on the same diet as their mothers.

At 6 months of age, 4 male rats from each of the groups—20%w lard, 5%w lard, 20%w safflower oil + vitamin E, and 20%w safflower oil—were drawn randomly for behavior testing. The operator did not know the composition of the diets; the dietary groups were simply labeled A, B, C, and D: A represented lard 20%w; B, lard 5%w; C, safflower oil 20% + vitamin E; and D, safflower oil 20%w.

The rats were maintained at approximately 80 percent of their free-feeding body weights and tested under conditions of 48-hour food deprivation. Testing was conducted in a Skinner box

(Lehigh Valley operant chamber; Lehigh Valley Electronics, Lehigh Valley, Pa.). This device was provided with two manipulanda (bars) which operated a food delivery magazine placed midway between the bars. Noyes reinforcement pellets (40 mg) were delivered when appropriate responses were emitted. Contingencies between responses (bar depression), cue lights (on or off) and the delivery of reinforcements were automatically controlled. A cue light was available over each bar. Animals were first placed in the testing chamber for 30 minutes with both bars set to deliver a food pellet after one press. This procedure was continued for 5 sessions conducted every other day. Animals which had not by that time begun to bar-press spontaneously were shaped by hand. After that time the reinforcement contingency was switched to FR-4 (the rat received a reinforcement consequent to emitting a total of 4 bar presses on one or both of the bars). These tests lasted 15 minutes and were conducted every other day. Three such test sessions were conducted for each animal. There were no differences between the groups under FR-4 testing.

After FR-4 training, a discrimination procedure was introduced in which only responses on the bar over which a cue light was lighted would result in reinforcement. After every correct response there was a 50:50 probability that the light would switch to the other bar. The tests were also of 15 minutes' duration and conducted every other day. Three such tests were conducted.

Results

The average number of correct responses \pm standard deviation per rat for the 3 tests conducted under FR-4 discrimination for the 4 groups are tabulated in Table 4. Group D (safflower 20%w) exhibited significantly fewer correct responses ($P < 0.01$, Mann-Whitney U test). There were no significant differences among the other groups. Group D (safflower oil) exhibited a significantly lower percentage of correct responses ($P < 0.05$) on tests 2 and 3 but not on test 1 (Table 4); there were no significant differences among the other groups.

To confirm these data, two additional groups of 4 rats each, labelled A and B, were given to the operator for evaluation. These rats were females, aged 9 months, and they had been given the semisynthetic diets since age 2 months. As in the case of the 6-month-old rats, there were no differences among groups under FR-4 testing.

The number and the percentages of correct responses under FR-4 discrimination are shown in Table 5. Group B (20%w safflower) exhibited significantly fewer correct responses than Group A (20%w lard) ($P < 0.01$). The percentage of correct responses by Group B was significantly lower on the first test ($P < 0.01$) but the differences were not significant for tests 2 and 3.

Three-Month-Old Rats

Method

This study employed 3-month-old male rats. The rats, born of mothers from the groups re-

TABLE 4
Effect of Dietary Fat on Discrimination Learning at Age 6 Months (Sprague-Dawley Male Rats*)

Diet†	Number of Correct Responses		
	No. of Correct Responses \pm S.D.		
	Test 1	Test 2	Test 3
A. Lard, 20%w	359 \pm 283	463 \pm 152	350 \pm 350
B. Lard, 5%w	291 \pm 171	409 \pm 103	398 \pm 102
C. Saff., 20%w + 20 mg vit.E	314 \pm 179	519 \pm 177	705 \pm 292
D. Saff., 20%w	90 \pm 49‡	118 \pm 80‡	104 \pm 76‡

Percent Correct Responses

Diet†	% Correct Responses \pm S.D.		
	Test 1	Test 2	Test 3
A. Lard, 20%w	56 \pm 24	53 \pm 5	65 \pm 16
B. Lard, 5%w	59 \pm 12	55 \pm 8	60 \pm 5
C. Saff., 20%w + 20 mg vit.E	50 \pm 4	53 \pm 7	65 \pm 6
D. Saff., 20%w	49 \pm 7	46 \pm 5‡	43 \pm 17‡

* Born of mothers receiving the same diets.

† Four rats in each group.

‡ Significantly smaller, $P < 0.01$, than the value for the other three groups.

TABLE 5
Effect of Dietary Fat on Discrimination Learning at Age 9 Months (Sprague-Dawley Female Rats*)

Diet†	Number of Correct Responses		
	No. of Correct Responses \pm S.D.		
	Test 1	Test 2	Test 3
A. Lard, 20%w	166 \pm 144	190 \pm 88	400 \pm 78
B. Safflower, 20%w	16 \pm 16‡	145 \pm 64‡	162 \pm 76‡

Percent Correct Responses

Diet†	% Correct Responses \pm S.D.		
	Test 1	Test 2	Test 3
A. Lard, 20%w	59 \pm 28	50 \pm 20	80 \pm 27
B. Safflower, 20%w	26 \pm 16‡	61 \pm 19	73 \pm 25

* Diets started at age 2 months.

† Four rats in each group.

‡ Significantly less, $P < 0.01$, than the value for Group A.

ceiving 20%w lard, 20% safflower oil+vitamin E, or 20%w safflower oil, as well as from mothers fed standard laboratory chow pellets (Rockland), were maintained with the same diet as their mothers. As before, except for the Rockland group, the operator did not know the composition of the diet. The diets were labeled A, B, C, D: Group A, Rockland; Group B, 20%w lard; Group C, 20%w safflower oil+vitamin E; and Group D, 20%w safflower oil.

The animals were tested in the operant chamber in the same manner as in Experiment 2A.

Results

Only in one aspect of the operant behavior testing was there a reliable effect of diet. This influence was on the percentage of rats spontaneously shaping; the values for the Rockland, 20%w lard, 20%w safflower oil+vitamin E, and 20%w safflower oil groups were, 76, 78, 95 and 25 percent, respectively. The 20%w safflower oil group was significantly poorer in this respect than the other three groups ($P < 0.01$). Responding under FR-4, or FR-4-discrimination, did not differentiate among the groups.

The earlier discrimination studies demonstrated that rats aged 6 months and 9 months in the safflower oil group, without the vitamin E supplement, had a severely depressed capacity to deal with the operant situation. With 3-month-old rats this suppression was evident only when the free shaping situation was considered.

DISCUSSION

Dietary fat did not significantly alter the lifespan of rats employed in the initial experiment with the Hebb-Williams maze or of those employed in the second experiment (20) with a Skinner box. However, in both studies, dietary fat modified learning behavior and, by implication, the functioning of the CNS. The results of both experiments are compatible with the possibility that enhancing the level of lipid peroxidation has an adverse effect on the CNS out of proportion to its effect on the body as a whole, as measured by mortality rate. Thus variation in the amount or degree of unsaturation of dietary fat and of factors (e.g., vitamin E) that can modify lipid peroxidation rates, may contribute to the variability in age of onset of evident degradative CNS changes such as senility, above and beyond the variations expected from differences in mortality rates.

The manner in which increases in the amount or degree of unsaturation of dietary fat modifies CNS function is unknown. Several mechanisms may be operating. Neuronal dysfunction may be mediated in part through deleterious effects of dietary fat on the glial cells. The rate of peroxidation of serum and vessel-wall constituents may be increased, leading to a more rapid development of arteriocalcapillary fibrosis (21). Increased lipid peroxidation in the synaptic areas, areas rich in polyunsaturated fatty acids (22) such as 22:6 ω 6 and 22:6 ω 3, could cause damage in a manner similar to that caused by β -hydroxy dopamine (23), or by the anesthetic, halothane (24, 25).

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FREE RADICAL THEORY OF AGING: EFFECT OF ANTIOXIDANTS ON THE IMMUNE SYSTEM

(By D. Harman, M. L. Heidrick, and D. E. Eddy, Departments of Medicine and Biochemistry, University of Nebraska, College of Medicine, Omaha, Nebr.)

Free radical reactions have been implicated in aging. Such reactions may contribute to the decline of the immune system with age and, in addition, to depression of antigenic responses through inhibition of the proliferative phase of the immune response, a period when cells display a heightened sensitivity to free radicals. In agreement with the latter are studies with Vitamin E, 2-mercaptoethanol (2-MEA), glutathione and dithiothreitol. The purpose of the present study was to expand knowledge of the effect of free radical reaction inhibitors on humoral response. C3HeB/FeJ female mice were obtained at weaning, caged 5/cage, and placed on a powdered diet (Rockland). At age 40 days each cage was started on a different diet by adding either nothing (controls, two cages), 0.25 percent w of either butylated hydroxytoluene (BHT), probucol (PB) (a derivative of 2,6-di-*t*-butylphenol), a quinoline derivative (Santoquin) (SQ) or, levamisole (LE), and 0.5 percent w of either Vitamin E (VE), 2-mercaptoethylamine (2-MEA), 2-mercaptoethanol (2-ME), or, NaH_2PO_2 (NaHP). At age 68 days each mouse was given an IP injection of sheep red blood cells. At age 73 days the mice were killed, splees removed and the humoral immune response assessed by the Jerne plaque assay. The average number of plaques \pm S.D. per group were: control, 460 ± 131 and 593 ± 103 ; BHT, 1051 ± 464 ; PB, 702 ± 272 ; SQ, 952 ± 430 ; LE, 965 ± 344 ; VE, 645 ± 252 ; 2-MEA, 1045 ± 344 ; 2-ME, 938 ± 352 ; NaHP, 843 ± 112 . These data support the possibility that endogenous free radical reactions have a deleterious effect on immune response. The data also suggest, as does its chemical structure, that the effect of levamisole on the immune system may be due to free radical reaction inhibition.

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FREE RADICAL THEORY OF AGING: EFFECT OF ANTIOXIDANTS ON HUMORAL AND CELL-MEDIATED RESPONSE AS A FUNCTION OF AGE

(By D. Harman, M. L. Heidrick and D. E. Eddy, Departments of Medicine and Biochemistry, University of Nebraska, College of Medicine, Omaha, Nebr.)

Free radical reactions, implicated in aging, may contribute to the decline of the immune response with age. If so, free radical inhibitors might delay the decline. To evaluate this possibility 0.25 percent w (by weight) of either α -tocopherol acetate (Vit. E) or a quinoline derivative (Santoquin) were added to the diet of C3HeB/FeJ female mice starting at age 40 days. At age 7, 10, 13, 16, 19, and 22 months 8

mice in the control and antioxidant groups were killed, spleen sections removed and combined, and the humoral (Mischell-Dutton splenic culture and Jerne plaque assay) and cell-mediated (Con. A: ^3H -thymidine) responses assayed. The humoral response data are given below; the cell-mediated data are similar.

Age (months):	Vitamin E		Humoral: AFC/culture Santoquin	
	AFC ¹ /Cult.	Percent of Cont.	AFC/Cult.	Percent of Cont.
7	584	175	887	266
10	1,689	189	1,148	129
13	3,231	206	3,085	197
16	2,742	155	431	24
19	443	33	794	59
22	817	563	237	168

¹ AFC-Antibody forming cells.

These data support the possibility that endogenous free radical reactions have a deleterious effect on the immune response and that addition of antioxidants to the diet may aid in offsetting the normal decline of the immune response with age.

UNIVERSITY OF EDINBURGH,
DEPARTMENT OF MEDICINE,
May 18, 1977.

Senator GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs, U.S.
Senate, Washington, D.C.*

DEAR SENATOR MCGOVERN: I am responding to your letter of May 2, 1977 with which you were kind enough to send a copy of the Senate Select Committee on Nutrition and Human Needs recently issued publication, *Dietary Goals for the United States*. You kindly invite me to comment.

I think the best way of doing this is to send you a prepublication text of a lecture which I have recently delivered at a international symposium held in the U.K., under the auspices of the Rank Prize Funds Committee, entitled "Diet of Man—Needs and Wants".

While agreeing in principle with your Committee's recommendations, it is my assessment that they go too far and beyond the point where there is firm supportive scientific evidence in that they are directed unselectively at the whole community.

I do not consider that it is wise to quote uncritically the recent survey conducted by Dr. Kaare Norum of the University of Oslo Medical School. I took part in this survey and the structure of the questions were such that doubts could not easily be expressed. A firm positive or negative was called for and some questions have had a built-in bias in favour of an answer relating diet to coronary heart disease.

I see no reason to shift my opinion from the statement in the accompanying paper "it is my belief that diet contributes to CHD mortality but that it is not the major component and not even the major com-

ponent within the environment. Furthermore, I suspect that the adverse effects that a diet rich in saturated fat might have are determined to a considerable extent by genetics susceptibility or resistance”.

Thank you for sending the report.

Yours sincerely,

M. F. OLIVER.

Enclosure.

DIET AND CORONARY HEART DISEASE

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“THE DIET OF MAN—NEEDS AND WANTS”

The relationship of diet to coronary heart disease (CHD) is a difficult scientific problem, since the facts do not lead to any cohesive or easy construction upon which firm conclusions can be based. In recent years it has been compounded by superficial and emotive interpretations. With over-extrapolation by some doctors and nutritionists who should know better, and partisan extension of the evidence by the public media, it is becoming increasingly difficult to keep the subject in perspective. Of course, I cannot guarantee to do this but, as a clinical scientist working in the cardiovascular field for 25 years, I will try to set some sort of balance.

It is my belief that diet contributes to CHD mortality but that it is not the major component and not even the major component within the environment. Furthermore, I suspect that the adverse effects that a diet rich in saturated fat might have are determined to a considerable extent by genetic susceptibility or resistance.

Recent epidemiology of coronary heart disease

This is a large and complex subject in itself and I shall only select a few points in order to emphasise the magnitude of the problem with which we are confronted.

First, CHD mortality in England and Wales, and in Scotland, has continued to rise steadily between 1969 and 1974 (the last available figures). The increase in CHD mortality has, apart from a temporary halt in 1968 and 1969, been continuous since 1950.

Second, in all of the United Kingdom, the rate of increase in CHD mortality in males is greatest in the 35–44 age group (80–100 percent). The rise in mortality in the 45–54 age group (60–70 percent) is also greater than that in the 54–64 age group (about 20 percent). Fig. 1 illustrates both points showing the changes in England and Wales. Since 1962, there has also been an increase in CHD mortality in women under 45 years.

Third, there are striking regional differences within the United Kingdom. These are illustrated in Fig. 2 where CHD mortality (standardized mortality ratios for the years 1969–1973) is indicated for men aged 45–54 on a map in relation to the population at risk (Fulton et al. 1977). The mortality rate in central west Scotland is nearly three times that of the south east of England. Similar gradients in CHD mortality apply to younger males, and to females (Fig. 3). The same is true for cerebrovascular disease mortality. The accu-

racy of representing differences in mortality on a demographic basis depends upon the reliability of death certification. This is always a weakness of such studies but there are not very major differences in the teaching of diagnostic criteria in the medical schools in this country and the International Classification of Diseases provides a fairly reliable standard for death certification.

Fourth, there has been a steady reduction in CHD mortality in the United States in both sexes, in each of the four decades between 35 and 74 and to the same degree in white and black people (Table 1). The explanation of this is unclear. While there has been a small fall in serum cholesterol (range 0.8–2.6 percent) between 1960/62 and 1971/74 at all ages and both sexes (Advancedata, 1977), there has also been a decrease in cigarette smoking and better control of hypertension.

It is difficult to see how a change in diet, particularly a change in a particular dietary constituent, can explain (1) the differential increase in CHD mortality by age in the United Kingdom (2) the regional differences in CHD mortality in the United Kingdom (3) the fall in CHD mortality in all sectors of the U.S. public.

Risk factors and genetic influences

The common risk factors for CHD mortality are well known. U.S. Inter-Society Commission for Heart Disease Resources (1970)—the Pooling Project is probably the best source of information and has clearly shown that raised serum cholesterol concentrations, raised blood pressure and cigarette smoking all separately increase CHD mortality and, in aggregation, increase the risk proportionately more than any one or two factors alone. Physical inactivity should also be included as a risk factor (Morris et al. 1973). It is not widely appreciated, however, that the survival rate over a 10 year period for the worst category—when all three risk factors are present—is 93 percent (Table 2). In other words, the risk of CHD for the high risk group is not in absolute terms very high.

A fundamental change in diet could only be expected to influence one of these three major risk factors, namely elevated serum lipids. Completely successful control of all three risk factors (if possible) is unlikely to return a middle-aged man's status of risk to that existing in those who have never had any risk factor present, since a considerable degree of atherosclerosis will already have developed.

There are other influences to take into account. In the Stockholm prospective businessman's study (Carlson and Bottiger, 1972) serum triglyceride concentrations were shown to be at least as important as serum cholesterol concentrations as correlated with CHD mortality, particularly in men under the age of 60. Serum triglyceride concentrations had largely been ignored before this study mostly because techniques for their estimation were not firmly established until about 1967. This relationship between serum triglycerides and CHD mortality is important because dietary triglycerides are likely to be of much greater importance than dietary cholesterol as pathogenic influences for atherosclerosis (see below).

Genetic factors still do not, in my opinion, receive sufficient attention. The concordance rate for CHD mortality is significantly greater in monozygotic twin pairs than in dizygotic twin pairs (Harvald and

Hauge, 1965). The concordance rate for serum cholesterol concentrations, likewise, is significantly greater in monozygotic twin pairs than dizygotic twins (Pikkarainen et al, 1966). It has been calculated that the heritability of serum cholesterol is between 35 and 40 percent (Slack, 1972). It is interesting also to note that the similarity of serum cholesterol concentration in families is significantly higher between siblings ($r=0.37$) when compared with that of husband and wife ($r=0.01$) (Schaefer et al, 1958). Genetically-determined abnormalities in cholesterol metabolism can play a significant role in the premature onset of the CHD and there are many reports of this disease developing in individuals with the single gene-determined familial trait of hypercholesterolaemia.

Diet

Any pathogenic association of diet with CHD must either show that a given dietary constituent leads to atheroma or to intravascular thrombosis or both. An excess of dietary saturated fat fulfills both roles, but dietary cholesterol fulfills neither.

A. Dietary saturated fat

Most of the evidence positively correlating dietary saturated fat with CHD mortality has been derived from comparisons between relatively undernourished or underprivileged communities with rich, over-nourished and affluent populations. The best known of these are the Seven Countries Study (Keys, 1970), the multi-racial Community Survey in Cape Town (Bronte-Stewart et al., 1955) and a number of studies of immigrants from poor to rich areas (Toor et al., 1957). The Seven Countries Study showed no correlation between the intake of total calories and CHD incidence ($r=0.004$), a weak correlation between the intake of dietary fat ($r=0.38$) and CHD, and a highly significant correlation ($r=0.84$) between the intake of dietary saturated fatty acids and CHD incidence. No significant correlation could be shown between the intake of dietary cholesterol and CHD incidence.

In spite of this rather convincing evidence, there is no indication that the intake of dietary saturated fat can be correlated with CHD mortality *within* developed communities where, for example, fat already comprises more than about 35 percent of total calories. Indeed, it is hard to conceive how the very minor variation in dietary saturated fat between the South and the North of the U.K. could contribute much, if anything, to the striking gradient in mortality previously discussed.

For the purposes of this discussion, dietary fat can be regarded as dietary triglyceride and it is the fatty acids esterified with glyceride-glycerol with which we are primarily concerned. Many who propose a strong relationship between dietary fat and CHD have failed to give adequate consideration to the complex metabolic processes which determine the oxidation, transport, re-esterification and storage of absorbed triglyceride fatty acids. For example, the lipoprotein lipases which are enzymes responsible for the metabolism of ingested triglycerides may be at least as important in the clearance of saturated fat from the plasma as the quantity of dietary fat itself. These considerations will be more explicit when discussing dietary cholesterol.

B. Dietary cholesterol

Diets which are high in saturated fat are usually high in cholesterol. The ordinary mixed diet in the U.K. contains between 1.0 and 1.6 mmol (400 and 600 mg) cholesterol daily and the chief source is the egg, which contains about 0.6 mmol (250 mg) according to size. Other common sources are milk, liver, shellfish and meat. At this level of consumption about 60 percent of cholesterol is absorbed. With higher intakes, the percentage of absorption falls and so a daily intake of as much as 7.8 mmol (3 g) can, for example, lead to the acquisition of only about 2.6 mmol (1 g) per day. The amount of cholesterol absorbed is affected by other constituents in the diet, particularly dietary fibre, the form in which cholesterol is presented and perhaps by genetic influences determining absorption of sterols.

Small changes in consumption of dietary cholesterol, such as fluctuations between 250 mg and 1.5 g, have no measurable effect on plasma cholesterol concentrations. Extremes of cholesterol intake, either as a result of eating 10–12 eggs a day or of taking no eggs, do alter plasma cholesterol concentrations but even these dietary influences tend to have only a transient effect before a new homeostatic balance is achieved.

The relationship between dietary cholesterol and CHD is remote in view of the effects of many other influences on plasma and arterial cholesterol and the importance of other risk factors (Oliver, 1976).

Plasma lipids

The intermediaries between dietary lipids and arterial lipids are the plasma lipids. It is necessary, therefore, to consider briefly some of the influences which determine their concentration and, in so doing, bear in mind that these influences are constantly being adjusted in the normal individual in order to maintain a steady state—the “*vie constante*” or “*milieu intérieur*” of Claude Bernard (1865). The homeostatic influences of endogenous synthesis, lipoprotein transport, tissue esterification and lipolysis, and endogenous catabolism are of far greater importance than the actual amount of dietary lipid presented for assimilation into the body.

Plasma cholesterol

The lipid in atheromatous arterial lesions is principally cholesterol, and hence the influences which determine plasma cholesterol concentrations are important.

The cholesterol circulating in the plasma represents about 10 percent of the total body pool of cholesterol. The plasma concentrations of cholesterol are determined by (1) the amounts synthesized in the body (2) the rate of catabolism and excretion in the bile (3) the equilibration between plasma and tissues and (4) the amount absorbed from the diet—probably in this order of importance.

The correlation between plasma concentrations of cholesterol and tissue concentrations of cholesterol is weak (Goodman and Noble, 1968). There are two large pools of tissue cholesterol, possibly three, with very low turnover which are independent of the rapidly exchangeable plasma pool (Samuel and Lieberman, 1973). The enterohepatic circulation of bile acids is very important in adjusting the body's reaction to variations in exogenous cholesterol intake and can act in a protective role.

Thus, estimation of plasma concentration of cholesterol gives only a crude reflection of tissue cholesterol concentration and this includes arterial tissue.

Plasma lipoproteins

Deposition of cholesterol in arterial tissue is determined by two main influences. One is the kinetics of lipoprotein interaction in plasma and of their relation to endothelial cells. The other is the efficiency of the metabolism of the arterial wall itself.

Cholesterol is an essential constituent of every cell. Its transport in plasma is dependent upon the availability and metabolism of specific apoproteins. Its transport into the cell is partly determined by the concentration of these cholesterol-rich lipoproteins (low density lipoproteins or LDL) and partly by the concentration of smaller lipoprotein moieties (high density lipoproteins or HDL). The latter may be "protective" lipoproteins preventing excess cholesterol deposition by acting as a substrate for enzymes responsible for esterifying deposited free cholesterol or by acting as competitors at receptor sites for LDL uptake. The kinetics of exchange of cholesterol and triglyceride between the different lipoprotein fractions has been a subject of intense research during the 1970s and more will undoubtedly be learned about the particular homeostatic mechanisms involved. It is sufficient, in this context, to point out that these are important influences which can act to protect tissues against excessive fluctuation in dietary lipid.

There is new epidemiological evidence to indicate that the positive correlations between plasma cholesterol concentration of LDL concentration with CHD mortality are both of a lower order than that of the negative correlation between HDL concentrations and CHD mortality (Gordon 1976) (Table 3). This raises an entirely new set of questions, emphasises the potential importance of "protective" lipoprotein concentrations and points out the simplistic approach of relating plasma cholesterol concentrations to CHD mortality of the last decade.

The importance of HDL is not likely to be settled for some years. Briefly, the evidence is that HDL promotes cholesterol efflux from tissues *in vitro*; body cholesterol pool size is negatively correlated with plasma HDL cholesterol; CHD frequently is associated with a low HDL cholesterol; situations characterised by high HDL are also associated with low CHD incidence; and all major conventional risk factors (except hypertension) are associated with a reduced plasma HDL (Miller and Miller, 1975).

The Edinburgh-Stockholm study of metabolic risk factors

This collaborative study provides new information about lipoprotein concentrations and of potential dietary influences in two cities with strikingly different CHD mortality. In men aged 40, the CHD mortality in Edinburgh is approximately three times that in Stockholm and 3 years ago we made a preliminary investigation to find possible explanations (Oliver et al, 1974). Last year we conducted a much more complex study of two random samples of healthy men, born in 1936 (aged 40). The results are not yet published and I will only describe those with the greatest relevance to this symposium. The random nature of the sample has been cross-checked and in Edinburgh there were

107 men studied (representing 73 percent of those selected) and in Stockholm 86 men were studied (representing 77 percent of those selected). All laboratory analyses were carried out "blind" in the same laboratory.

There were several important and significant findings in the plasma lipid analyses related to CHD (1) the mean serum cholesterol concentrations of both populations were below 220 mg/100 ml (2) serum cholesterol concentrations and LDL cholesterol were identical in Edinburgh and Stockholm men (3) serum triglycerides and VLDL triglyceride were significantly increased in Edinburgh men (4) serum triglyceride fatty acids and the fatty acids of adipose tissue were significantly more saturated (low P/S ratio) in Edinburgh men compared with Stockholm men (5) adipose tissue of Edinburgh men was particularly deficient in linoleic acid (6) there were more men in Edinburgh with low concentrations of HDL and more men in Stockholm with higher concentrations of HDL. Full dietary analysis is complex and has not yet been completed, but the differences in adipose tissue cannot reflect recent dietary habits, since it takes 1½ years to achieve any major change in the P/S ratio in adipose tissue as a result of alteration of dietary P/S ratios. Nevertheless, these findings support the view that communities with low dietary P/S ratios have a high CHD incidence.

There was no significant difference in weight or fat cell size, but Edinburgh men were significantly shorter than Stockholm men.

In addition, there was a greater insulin response to a glucose load; more cigarette smoking; higher systolic and diastolic blood pressures; and more physical inactivity in Edinburgh men.

Regression studies

Atheroma.—Evidence often adduced in support of a positive relationship between dietary cholesterol and atheroma is based on the fact that experimental feeding of diets rich in cholesterol can lead in some species to an increase in plasma cholesterol and to arterial lesions. Regression of these induced lesions occurs when the diet is returned to normal. Such studies conducted in primates have been used as sufficient evidence to reduce dietary fat in man. My interpretation is entirely different.

Lesions produced in monkeys by these diets resembled atheroma (Armstrong et al. 1971) but they are conspicuous by the absence of thrombus formation and platelet-fibrin incorporation into the plaques. Cholesterol is a very sclerogenic substance and it might be expected to produce a low grade inflammatory response with collagen and fibroblast reactions, but it is a big jump to call this atheroma. The results of these experiments should be recorded as factual experience in relation to the experimental situation under which they were made. No additional interpretation should be given. The contribution of dietary cholesterol to the normal mixed human diet is a fraction of that which was given to these animals. The plasma concentrations in man are also a fraction of the levels produced in these animals. The conditions did not mimic the exposure of man to slight rises of plasma cholesterol over many years. That the feeding of a diet very rich in cholesterol for a period of nearly two years leads to cholesterol-rich arterial lesions and that cessation of such a diet leads to regression of such

lesions does not, in my view, provide convincing enough evidence to change the constituents of the human diet.

Coronary heart disease.—There have been three major studies of the effects of reducing dietary saturated fat and substituting polyunsaturated fats on the incidence of CHD. One of these—the Anticoronary Club—was partly a secondary prevention trial and did not have any concurrent and adequately matched control group (Christakis et al. 1966). Another was a primary prevention trial conducted in an elderly population (Dayton et al. 1969). It showed a marginal reduction in CHD incidence in men under the age of 60, but the only statistically significant result which could be obtained was when CHD incidence was combined with that of cerebrovascular disease and other vascular diseases. A third study, the Helsinki Mental Hospital Study (Miettinen et al. 1972), also indicated that a diet rich in polyunsaturated fats reduced CHD incidence although not mortality. Unfortunately, there were weaknesses in design and conduct of this complex 12 year study. These include changes, which were not matched between the diet and control groups, in the individuals in the population studied; differences in the mental disorders in the treated and control groups; incomplete blindness of the doctors responsible for recording events; and inadequate follow-up of those removed from the study.

The fact that these three primary prevention trials all showed a trend in favour of reduced saturated and increased polyunsaturated fats has been used by some as sufficient evidence to advise that the whole community should have a major reduction in dietary saturated fat with a good deal of certainty of controlling the incidence of CHD. Unfortunately, the weaknesses of these studies are such that none of the findings, separately or together, justify such a sweeping conclusion. Equally, the establishment of a new diet-heart study would be such a monumental and vastly complicated exercise that it is unlikely ever to be done.

The results of the Lipid Research Clinic's trial of lowering hyperlipidaemia in severe heterozygotes (Types 2A and 2B) will be critically important in determining whether such action effects CHD incidence.

The situation is unresolved and is unlikely to be resolved. This encourages confused and confusing opinions. Evangelists who favour widespread reduction in dietary fat call for action now (Turner and Ball, 1974). Others demand more scientific evidence and see no justification in advising any change in diet (McMichael, 1976). My own appraisal is that there is insufficient evidence to warrant a change in the dietary fat consumption of the whole community—men, women and children of all ages—but that certain high risk groups with marked hyperlipidaemia may benefit, although even this lacks proof.

Meanwhile, the U.S. Senate Select Committee on Nutrition and Human Needs (McGovern Committee) has recently issued dietary goals (Fig. 4). Although deemed to be prudent, they go far by recommending a reduction of fat calories to 25–30 percent of total calories. This is directed unselectively at both sexes and all age groups and could have profound repercussions on individuals, families and the economy. Interestingly, the Committee advocates an absolute reduction in polyunsaturated and monounsaturated fats although the P/S ratio is increased.

Dietary sucrose

Epidemiological studies indicate that several populations with a high sucrose intake have a high CHD mortality. This dietary constituent also requires consideration in the aetiology of CHD (Yudkin 1963; 1972). The epidemiological evidence of the Seven Countries Study (Keys, 1971) shows that the correlation ($r=0.78$) between dietary sucrose and CHD mortality is of the same order as that for dietary saturated fatty acids and CHD mortality. But, if the data is calculated holding dietary fat consumption steady the correlation with dietary sucrose is lost, while a calculation holding dietary sucrose steady, continue to show the existence of a positive correlation between dietary saturated fat and CHD mortality (Keys, 1973). The situation is compounded by finding that there is often a positive correlation between the amount of sucrose consumed and cigarettes smoked.

The link between dietary sucrose and atheroma, if it exists, is likely to be through plasma triglyceride concentration. It has been shown in many short term experiments that added sucrose can increase triglyceride concentration. But comparison of sucrose with mixed starches under strictly isocaloric conditions did not produce any change in plasma triglyceride when the sucrose and starch were exchanged at ordinary levels of intake i.e. about 20 percent of total energy (Mann and Truswell, 1972). Induction and regression studies of atheroma have not been conducted on a formal basis and so no comment can be made concerning the atherogenic effects of dietary sucrose. There have been no dietary trials with high and low sucrose diets comparable to those studying the effects of dietary fat on CHD. A study was conducted by the Medical Research Council (1970), which showed that there was no difference between dietary sucrose intake in patients with CHD compared with controls.

Dietary fibre

It has been suggested that dietary fibre may protect against CHD by lowering plasma cholesterol. Different dietary fibres have strikingly different effects and, for example lignin and pectin produce reduced plasma cholesterol levels over a period of a few weeks but, wheat fibre, cellulose and various gums have little effect on plasma cholesterol in man. Formal epidemiological evidence relating dietary fibre intake to CHD incidence is not available.

Soft water

While it seems clear that the incidence of CHD is higher in soft water areas (Crawford and Crawford, 1967) it is still not understood what component in soft or hard water could be responsible for this. There is no very convincing evidence that any of the expected risk factors are different in cities with soft and hard water and, in particular, plasma lipid concentrations are not strikingly different. I do not understand the "water story" and really do not feel competent to comment more. I find it difficult, however, to see how it could be a major component in the changing incidence or the geographical distribution of CHD mortality.

Conclusions

The only dietary constituent with a sound relationship to CHD is saturated fat. The relationship is dependent, however, on many variables and not the least of these is the remarkable homeostatic pro-

tection of our bodies against the possible adverse effects of excess dietary saturated fat. While a case can be argued for the reduction of dietary saturated fat in certain categories of individuals, we are not going to cure coronary heart disease by altering the fat content of the diet of the whole community. There are other equally important environmental factors operating to produce CHD, such as cigarette smoking and physical inactivity. Genetic susceptibility and resistance are influences of obvious importance.

Our responsibility is to keep the balance between our wish to do good and the maintenance of sound judgment. Certain simple dietary measures should be introduced for the benefit of the public's health and these have already been listed in detail by the Report by COMA (1974) and the RCP/BCS Working Party (1976). Essentially, they comprise a reduction in total calories and saturated fat for those under the age of 55 or 60. Complex dietary measures are justified for those particularly at risk. These are (1) the siblings and children of young patients with CHD (2) individuals with familial hypercholesterolaemia and their siblings and children (3) young individuals with a number of risk factors such as hypercholesterolaemia, hypertension, excess cigarette smoking and physical inactivity. In such categories, saturated fat should be reduced below 35 percent of total calories and the P/S ration adjusted to be above 1 or 1.5.

Finally, we should be modest with our conclusions concerning the importance of dietary constituents with regard to the incidence of CHD. There is insufficient evidence to ascribe the secular and geographic trends in the U.K. in CHD mortality to diet, and insufficient evidence to make radical change unselectively in the hope of reducing CHD mortality.

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TABLE 1.—PERCENT CHANGE IN HEART ATTACKS DEATH RATES PER 100,000 POPULATION, UNITED STATES, 1968-74

Age group	White	
	Male	Female
35 to 44.....	-20.6	-20.1
45 to 54.....	-13.3	-14.4
55 to 64.....	-14.6	-15.0
65 to 74.....	-14.4	-20.3

Source: Adapted from Gordon & Thom, 1975.

TABLE 2.—10-YEAR AGE-ADJUSTED RATE PER 1,000 MEN AT RISK

Risk factors	1st major event	10-year survival (percent)	
		CDH death	
None.....	20	13	99
C+H.....			
C+S.....	89	36	95
H+S.....			
C+H+S.....	171	82	93

KEY TO SYMBOLS

C=serum cholesterol>250 mg/100 ml.

H=diastolic blood pressure>90 mmHg.

S=any cigarette smoking.

Source: U.S. Inter-Society Commission for Heart Disease Resources, 1970.

TABLE 3.—THE RELATIVE IMPORTANCE OF DIFFERENT LIPIDS AND LIPOPROTEINS AS PREDICTORS OF CHD.

	Likelihood ratios	
	Males	Females
Low HDL cholesterol.....	14.0	21.2
High LDL cholesterol.....	4.4	4.5
High total cholesterol.....	2.0	2.3
High triglyceride.....	.5	9.5
HDL/total cholesterol.....	17.1	20.4

Source: Framingham Study and Gordon et al. 1976.

PERCENTAGE
CHANGE

MALES

Age in yrs. Rate/100,000 1950-52

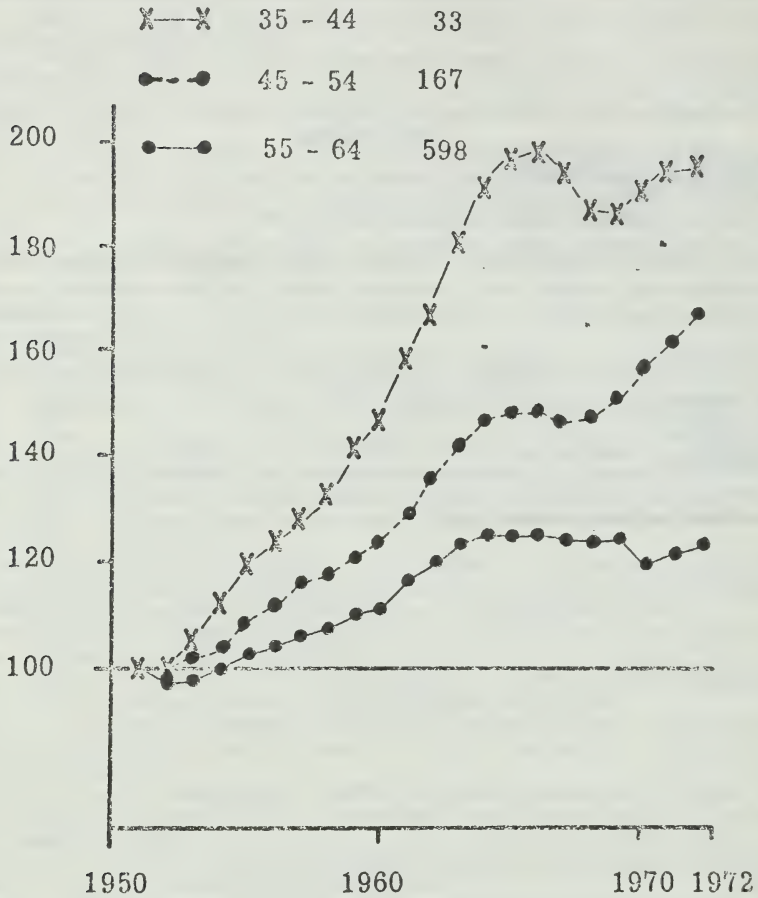


FIGURE 1.—Percentage change in death rates in three age groups (from 35 to 64 years) from ischaemic heart disease in England and Wales, 1950-73. (Three-year moving averages with 1950-52=100).

ISCHAEMIC HEART DISEASE (ICD 410-414) MALES 45-54

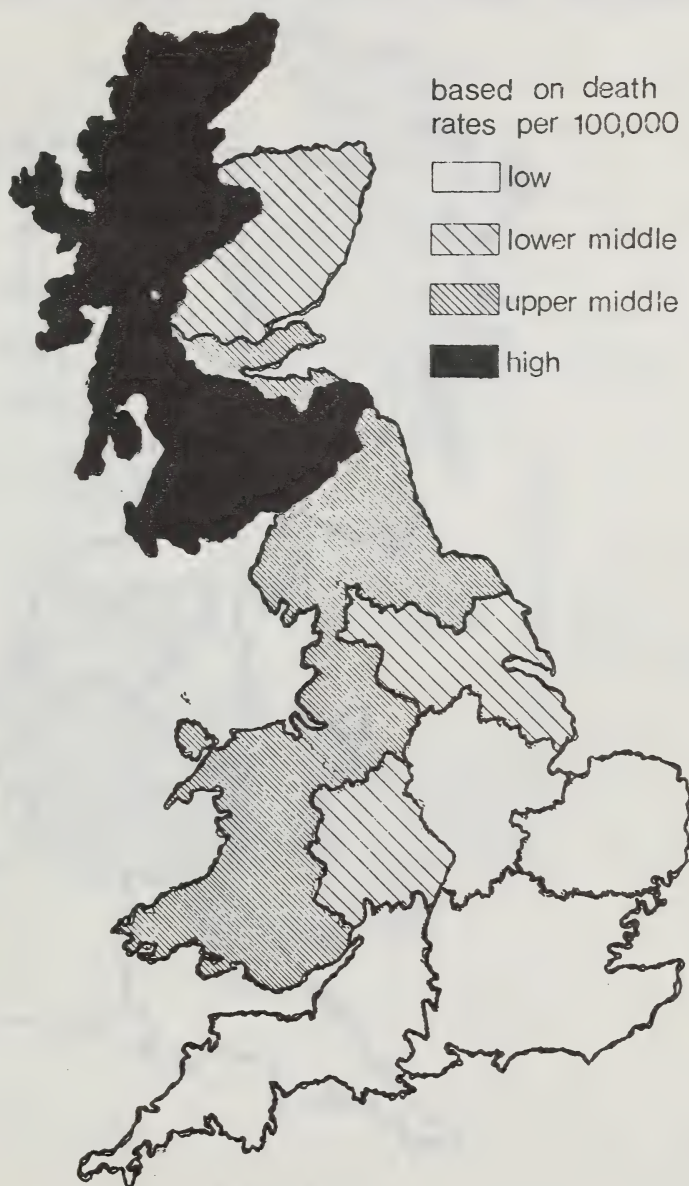


FIGURE 2

ISCHAEMIC HEART DISEASE (ICD 410-414) FEMALES 45-54

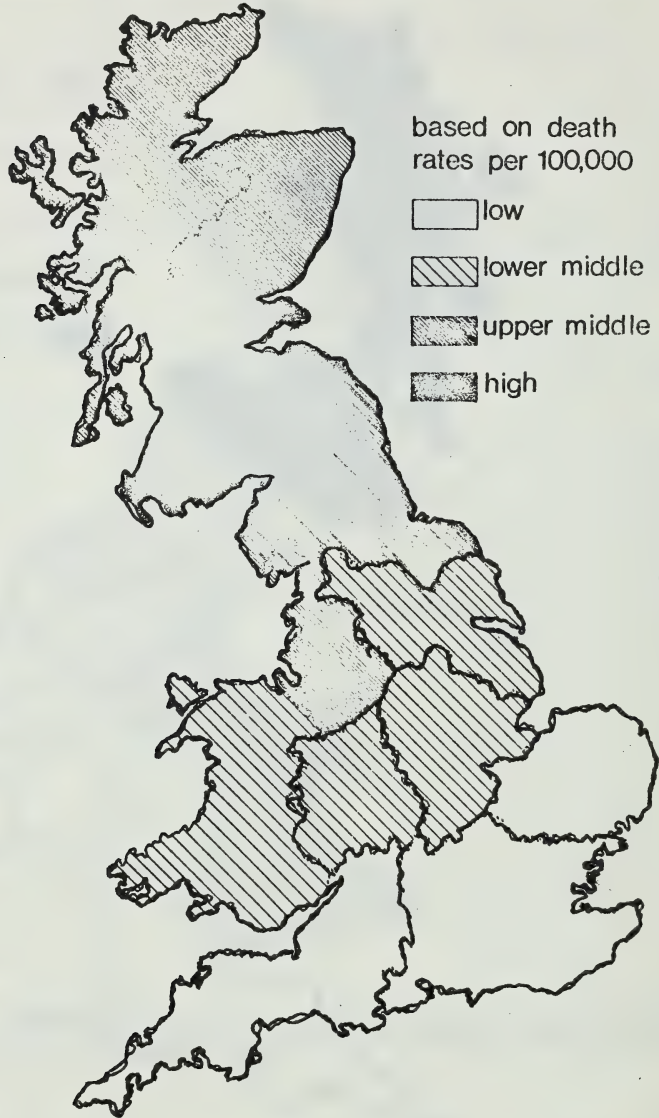


FIGURE 3

U.S. DIETARY GOALS
(McGovern Senatorial Committee - 1977)

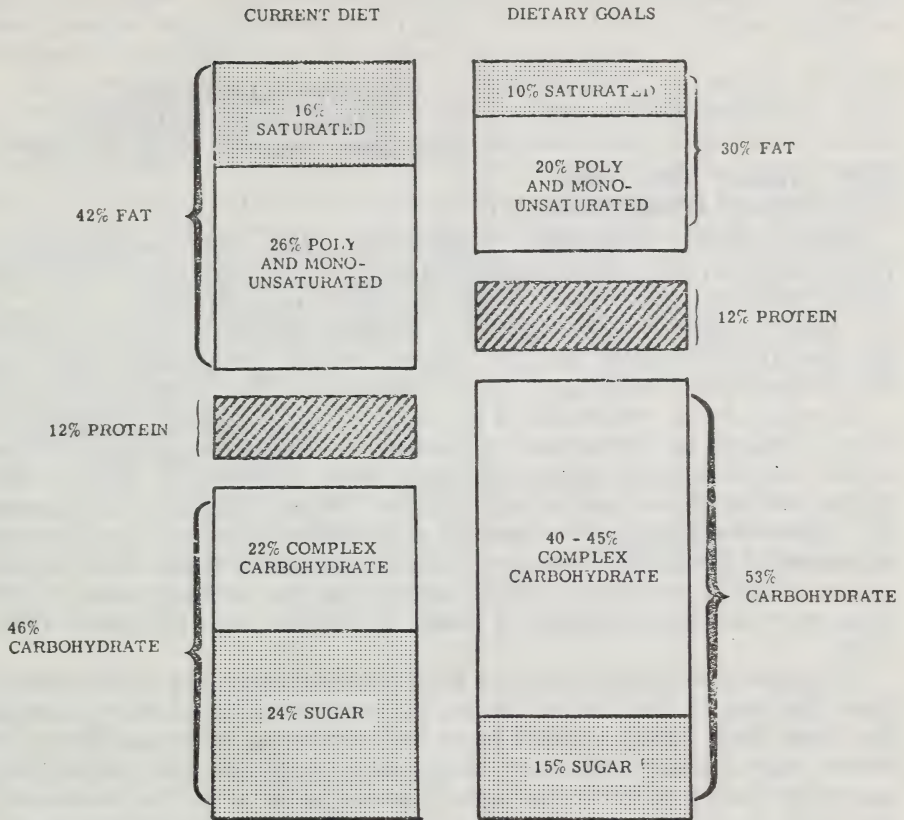


FIGURE 4

SERAFIMERLASARETTET,
MEDICINSKA KLINIKEN,
Stockholm, Sweden, May 16, 1977.

Hon. GEORGE MCGOVERN,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN, I thank you very much for the honour bestowed upon me by being asked to answer some questions in relation to the publication "Dietary Goals for the United States".

I take the liberty of sending you together with this letter a copy of my two Lilly Lectures in 1974 concerning the problems of coronary heart disease and dealing to some extent with the possible measures to be taken by governments. The second lecture delivered before the Royal College of Physicians in London is, therefore, labeled "What to tell our statesmen about ischaemic heart disease?" A part of this paper derives from discussions with our former Minister of Finance, Mr. Gunnar Sträng, who was in an earlier period of his life also Minister of Social Welfare and Health. Enclosed I am also sending you a recently prepared graph concerning the developments of the diet, or rather consumption of food, in Sweden over the years 1960-1976.

My general feeling is that the food problems are very much smaller than they are in the United States. It has always struck me, during the more than thirty years I have been traveling back and forth between your country and mine, that young people in your country are more fat than ours of similar age. It seems to me as if they were overfed both in childhood and later on in adolescence. In earlier years I was very much interested in the possibilities of changing peoples food habits. I have studied some American papers and we performed similar investigations in the south of Sweden where I was working at that time. I am sending you a copy from this paper (unfortunately in Swedish but perhaps somebody can translate it?*) because we found out that those who determined what to be eaten at home at that time was in the upper and lower social classes the children and in the middle class families the husbands and in no family the wife. The point of view of health as a deciding factor was forwarded more often in social class one whereas taste and tradition seems to be more prevalent in other social groups.

I am very much in doubt whether a less than radical change in the food habits is going to have any noteworthy effect on the state of health of the people. However, anything that can make people slimmer will also probably make them more effective and certainly it would be good from the point of view of economy, both the family's and the nation's in a global perspective. Moreover a return back to health habits, dating one or two generations back, would probably not be bad and probably less dangerous than the present food habits prevailing in the United States.

*See p. 599.

As I indicated in my second lecture I am rather doubtful concerning the effects of governmental advice on such personal matters as food. I do more believe in the example set by well known sportsmen (heroes) and people from the stage and public life whose example might influence the style of life of more than one generation.

As concerns my own country I believe that the points of view presented before your committee by Sir John McMichael from England very much resemble mine. But—as stated above—it may well be that the American food habits have gone so much further in the wrong direction that interference would be more relevant than in our country.

Since my Lilly Lectures was given, I have been elected Member of Parliament in my own country (where I am the only Physician and the only University Professor in the Parliament). I certainly appreciate being involved in an international undertaking like the one you perform, but I do not think that the views I expressed in 1974 have changed very much for my own part by participating in parliamentary work.

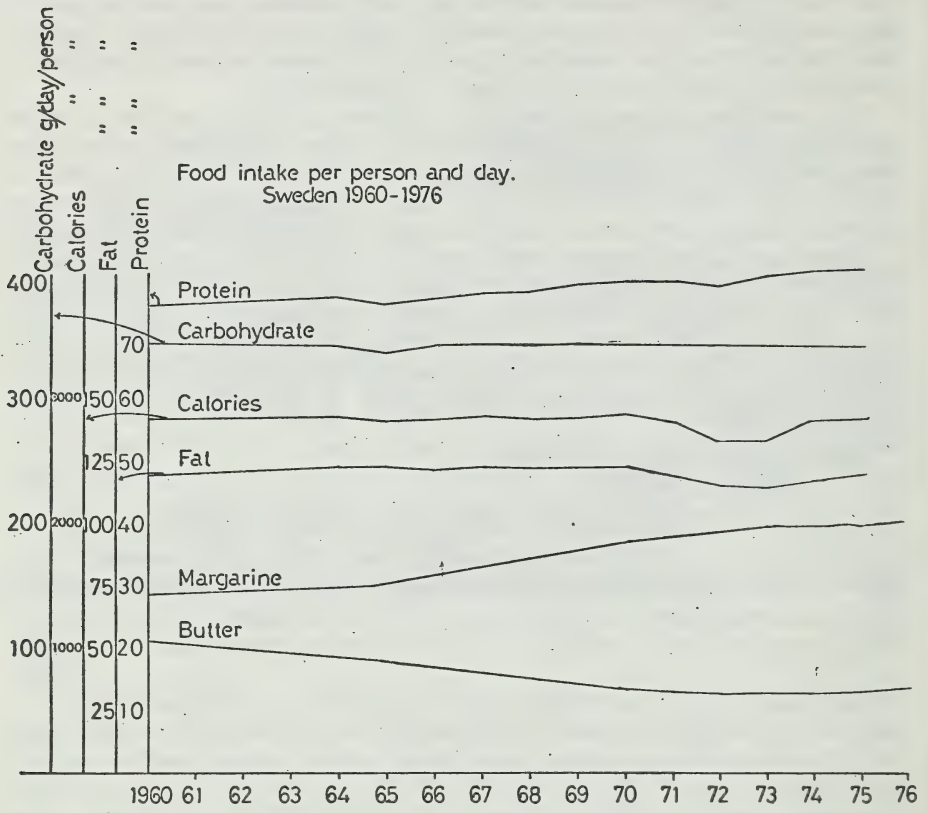
With all good wishes, I am Sir,

Sincerely yours

GUNNAR BJÖRCK, MD, FRCP, FACP (Hon.),

Professor of Medicine at the Karolinska,

Head of the Department of Medicine at the Seraphimer Hospital. . .



CONTRASTING CONCEPTS
OF
ISCHAEMIC HEART DISEASE

The 1974 Lilly Lectures
given at Oxford and London

by
GUNNAR BIÖRCK
M.D., F.R.C.P.

ALMQVIST & WIKSELL INTERNATIONAL
Stockholm-Sweden

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P r e f a c e

This book contains two Lilly lectures, given at Oxford and in London in November 1974. They represent an attempt to discuss problems connected with ischaemic heart disease, our concepts of the "disease" and its impact on society. Some of the views expressed here may be labelled heretical and nihilistic. The author is, however, well aware of the differences in the way this disease presents itself, and affects the populations in various countries. In this respect, data from England, Sweden and Finland have been used as illustrations in these lectures, given by a Swede to an English audience.

Although the lectures were organized in order to survey the different aspects indicated by their titles, a certain overlapping has been unavoidable. Each one is, however, a paper in itself. There is only one list of references, common to both papers. The oral presentations were somewhat abbreviated in comparison to the original text as presented here.

I thank the Royal College of Physicians in London for having invited me as their Lilly lecturer, and in particular its President, Sir Cyril Clarke, for all genuine interest, support and friendship shown to me on this occasion. I am also indebted to Doctor Ian Hunter, Senior Vice President of the College, and Doctor John Badenoch of Oxford for their help and understanding, as well as to miss I.S. Rawlings of the Royal College of Physicians.

My colleagues at the Seraphimer Hospital most generously took their time to read and criticize drafts of these lectures. Miss A.M. Bolander of the Swedish Central Bureau of Statistics and Mrs. Ira Eidensten were invaluable in providing the vital statistics material the way it appears in the illustrations. Mrs. Catherine Lagercrantz, likewise, has contributed in an inspiring way with the production of illustrations, typing and general organization of the material. Other secretarial work was provided

Gruvfält, miss Ann-Marie Lothigius, mrs. Margareta Jansson and mr. Joseph Biczok.

Grants from Karolinska Institutet and the Folksam Insurance Company contributed to the financing of this work. Support was also given by the Lilly Research Centre Ltd, England.

ISCHAEMIC HEART DISEASE -

A "MEDICAL" OR A "PSYCHO-SOCIAL" DISORDER?

With some reflections on the tasks
confronting clinical medicine

A Lilly lecture,
given on November 19th, 1974,
at the Radcliffe Infirmary, Oxford

The choice of a subject

A Lilly lecturer is supposed to give two lectures, one at the Royal College of Physicians in London and the other one in "a provincial town". It is left to the lecturer himself to decide whether he will give the same lecture in both places or two different lectures.

Although I am a clinician - or, perhaps, precisely because I am a clinician - I have never been able to look at medical research only as a laboratory undertaking. Instead, I have always considered medicine as a part of society, with strong interactions between the whole and its parts, and these, therefore, also being a subject for scientific studies. In this context, I set myself the task to discuss what our present medical knowledge of ischaemic heart disease as a community problem might imply in terms of political decisionmaking, and, thus, the lecture I am go give tomorrow at the Royal College of Physicians will deal with the question "What to tell our statesmen about ischaemic heart disease?".

During the preparation of that lecture it became evident to me that I ran into far more controversial material than I had anticipated, and that one hour's lecture would not allow for a reasonable presentation of the many basic controversies in our understanding of ischaemic heart disease - its etiology and the feasibility and consequences of its prevention. It, therefore, occurred to me that I might attempt to divide my subject in such a way that here, at Oxford, I would concentrate upon reporting some work done in - or in the neighbourhood of - our department of internal medicine, (as we say, or of clinical medicine, if you prefer that label) while I would try to deal with community aspects at the Royal College tomorrow.

I have tried to assemble some pieces from our work under a heading that may sound a little bit provocative - though not much so really - for Heberden and Hunter were aware of the problem, and Osler knew it by heart.

1. Quotation from a motion by the Center Party in the Swedish parliament 1973:

"Modern diseases like ulcer, asthma, goiter, hypertension and myocardial infarction have greatly a psychosocial etiology. They are often psychosomatic. One third of 60-70 million days of sickness are caused by stress and insecurity."

2. Quotation from WHO, Second Conference on Prevention and Control of Major Cardiovascular Diseases. Brussels, June 1973.

"Governments were asked to make provision for the implementation of the recommendations presented by the Conference."

Such recommendations were:

The community as a whole should be approached and helped to change the modern way of living as such.

Influence the adverse dietary habits of the population. Citizens should have the right to live in an environment unpolluted by the tobacco smoke. Emphasis should be placed on physical education throughout life.

Fig. 1

Public opinion.

Yet, at a time when one finds any enlightened layman - and quite a few of our colleagues - asking the medical profession to attack, and prevent, "unnecessary" disease at its grass-roots (1, 2), we are being forced to re-examine our concepts and the evidence behind them, in the light of our experience.

What do statistics tell?

Is it true that myocardial infarction is a psycho-somatic disease? Is it true, to quote another WHO document (3), that "this disease may therefore be an indicator of man's maladaptation to his civilization"? Or is it true that this disease - or these

diseases - are chiefly due to factors inherent in the human biochemistry as such?

Let us begin with a look at some hard facts, namely what epidemiologists call "end points". Death is one, and probably the safest, end point.

What has happened with deaths from all causes and from ischaemic heart disease in our countries over the last twenty years?

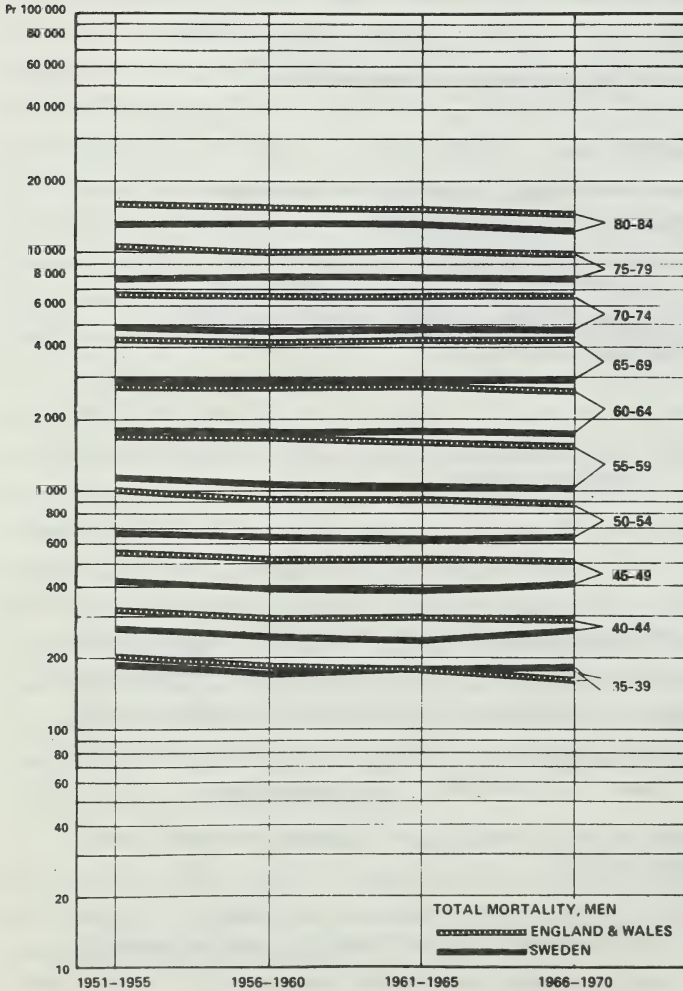


Fig. 2

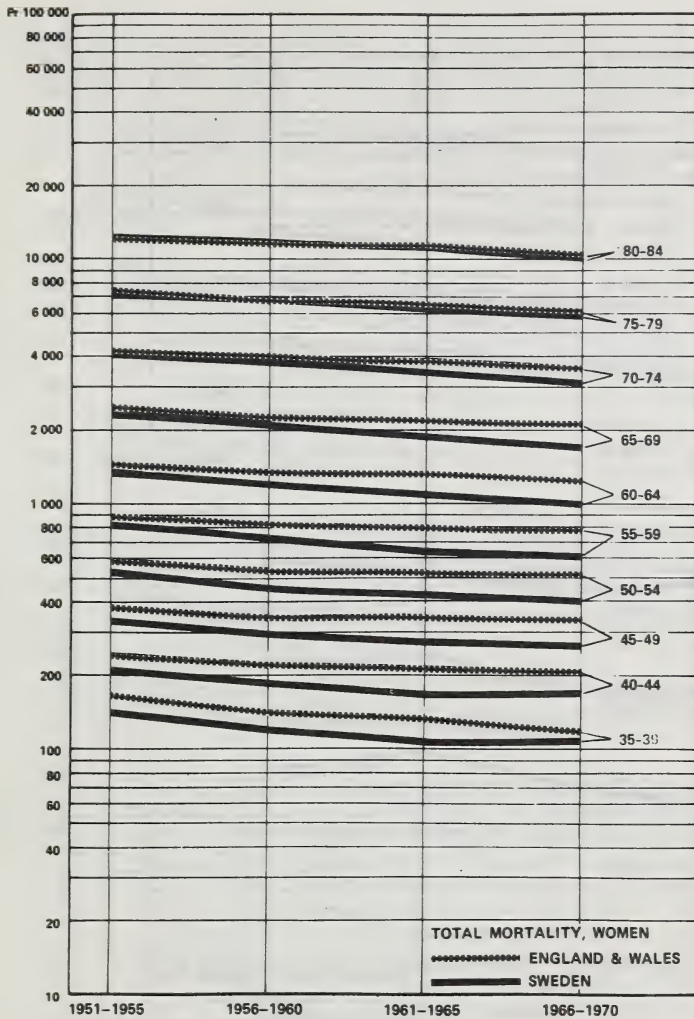


Fig. 3

Total mortality in our countries is decreasing for both men and women (figs. 2 and 3) but there are considerable differences in mortality rates in the same age groups between our countries, your figures, unfortunately, in most age groups being less favourable than ours (and, therefore, your life expectancy being shorter than ours).

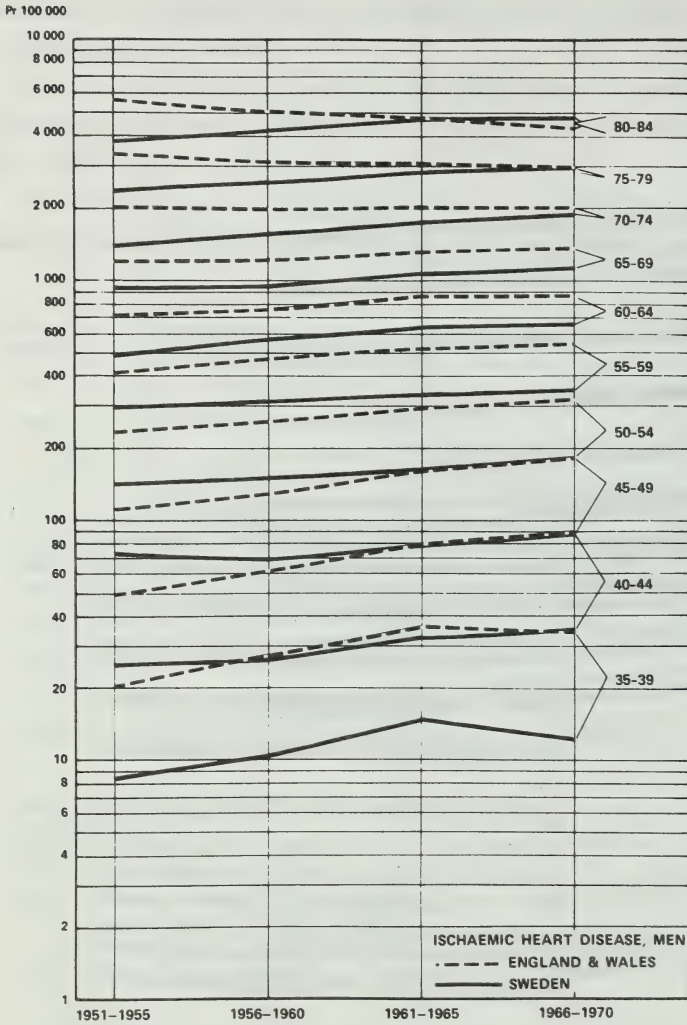


Fig. 4

Mortality from ischaemic heart disease (Figs. 4 and 5) is slightly decreasing for Swedish women of all ages and for English women above age 55. There is a modest increase for English men up

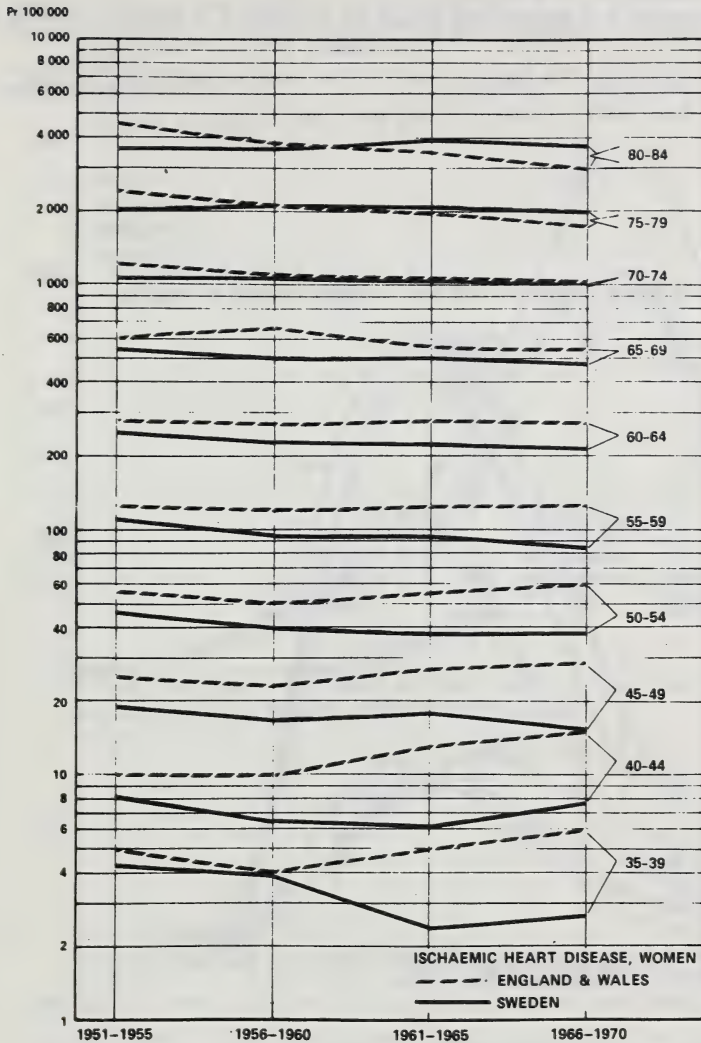
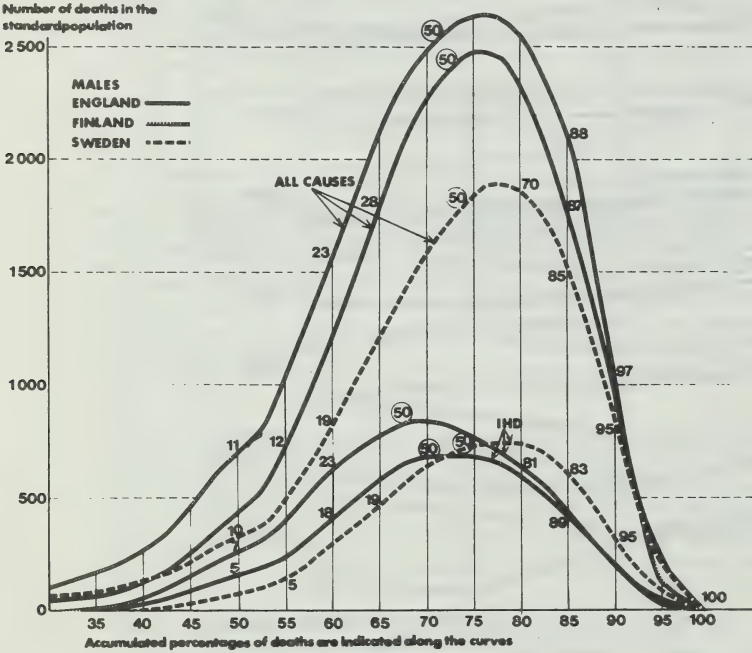


Fig. 5

to age 70 and very little change after that age. In Swedish men, there is an increase in all age groups of the size 1 per cent/year, part of which, however, may be due to changes in terminology and to the shift in cause of death in treated hypertensives.

If you look instead at the distributions - which are standardized with regard to age - of deaths from all causes and from ischaemic heart disease in England and Sweden (and, for comparison with Sweden, in our neighbour Finland), this picture emerges (Figs. 6 and 7):

AGE-DISTRIBUTIONS OF DEATHS FROM ALL CAUSES AND FROM IHD IN A STANDARD POPULATION, 1963-1971



AGE-DISTRIBUTIONS OF DEATHS FROM ALL CAUSES AND FROM IHD IN A STANDARD POPULATION, 1969-1971

Number of deaths in the standard population

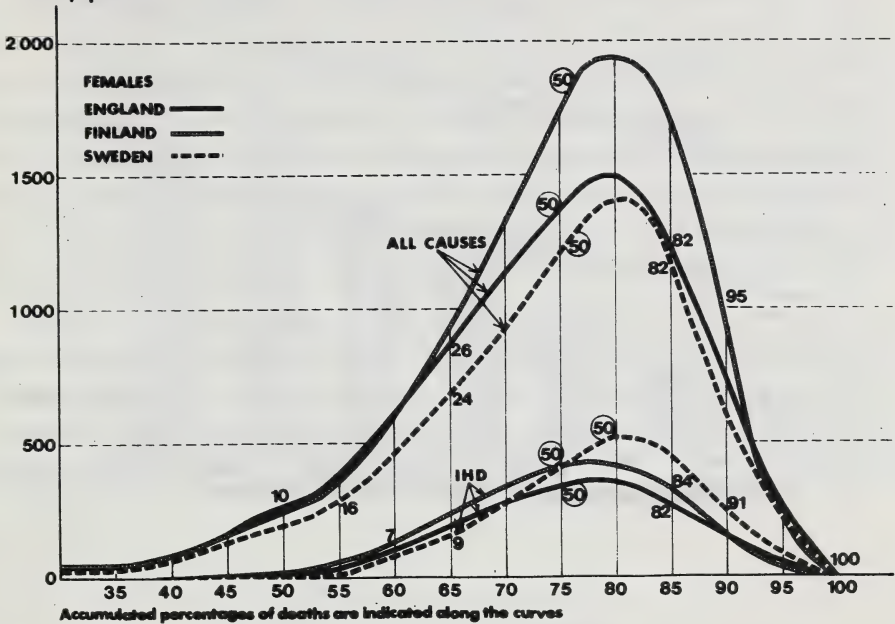


Fig. 7

Fifty per cent of all deaths have occurred, in England at about age 73 for men and age 75 for women, while the Swedish figures are 74 and 76. For ischaemic heart disease, the English figures are 71 for men and 76 for women, and the Swedish ones 75 for men and 79 for women. Thus, ischaemic heart disease as a cause of death strikes some years later than deaths from other causes in Sweden, while it strikes earlier in English (and Finnish) men.

I shall not here dwell upon the possible causes for these differences. But I want to stress that the impression we as hospital physicians have got of a heavy increase in myocardial infarction may depend in part on changes in the utilization of hospital beds over the last generation.

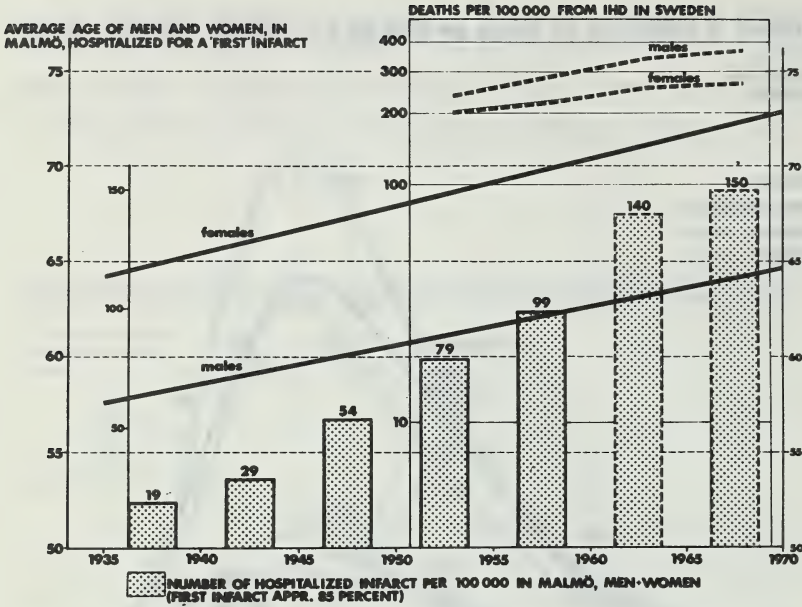


Fig. 8

A compound figure, derived mainly from data given by B.W. Johansson (4).

What has happened in our country is that we have got more infarct patients in the hospitals, but these patients at the same time derive from higher age groups than before, and this is true also of what is judged to be "first" infarcts.

In summary, at least from my post of observation, the massive impact of ischaemic heart disease is one in the decade around retirement age. In England, and even more in Finland and the U.S.A.,

however, the impact begins somewhat earlier than in Sweden, say, by five years or more.

These differences, are they due to various expressions of maladaptation or malcontent with regard to our "civilization", or are they expressions of genetic or other differences of our populations? I am not prepared to answer these questions. A review of even a small part of what has been written about these things would take far too much time. What I can contribute here are small pieces of research and observations derived from our department, mainly as spin-offs from our daily activities in the care for victims of this and other diseases. The clinical reality has provided us with a vast number of questions, some of which have been amenable to scientific study. These questions have, perhaps, undergone some transformation and some refinement over the years. Essentially, however, they remain the same.

Challenges to cardiology

A little more than thirty years ago I joined the forces of Swedish internal medicine, more specifically a division devoted to cardiology, headed by the late Gustaf Nylin. After half a dozen years in his department, I moved to the service of Jan Waldenström, where medicine was interpreted more in metabolic terms than in those of hemodynamics, and, after eight happy years in Malmö, in 1958 I was called back to Stockholm in command of that small but ancient medical fortress, named Serafimerlasarettet - The Seraphimer Hospital, founded in 1752 by the Swedish Royal Order of the Seraphim (Fig. 9).

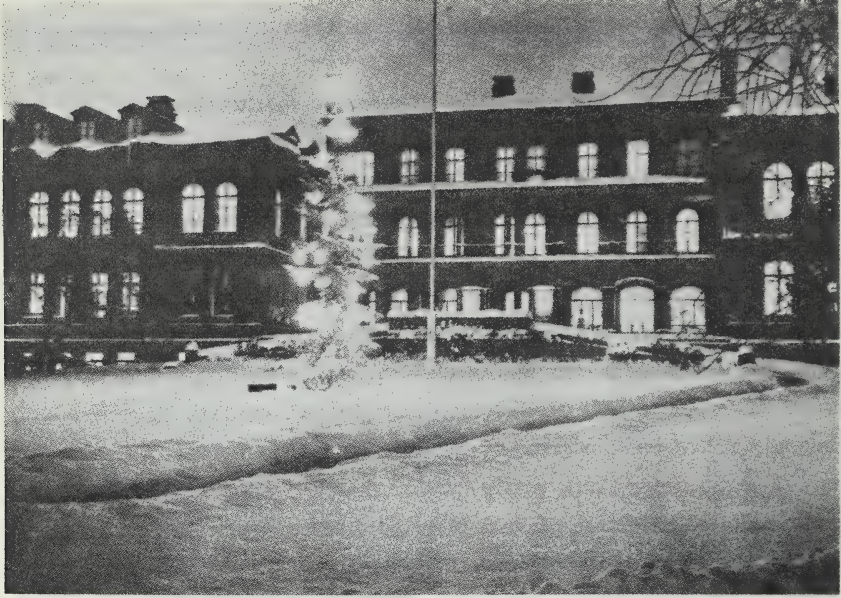


Fig. 9

The Seraphimer Hospital: Department of Medicine.

Thus, it has been my duty to promote the development of cardiology within the framework of internal medicine, and while the emphasis to begin with was clearly on cardiology, my responsibility in later years, no doubt, has been to reintegrate cardiology into the big machinery of internal medicine-at-large, and, perhaps, both of them into the world we live in.

In table I, I have tried to indicate some of the major subjects that have been in the focus of international cardiology over the last 30 years or more. I have been fortunate, at one stage of my career or another, to be connected with most of them in my daily work and in research activities. Half-way in this process, in 1959, I was given an opportunity to examine the state of affairs of our thinking and doing with regard to ischaemic heart disease (5).

The 1940's:

- x Chest leads and electrocardiographic provocation tests
- Cardiac catheterization and angiocardiology
- Surgery of congenital heart lesions

The 1950's:

- x Direct-writing electrocardiography and defibrillators
- Open-heart surgery and surgery of acquired heart lesions
- New diuretics for the treatment of cardiac failure and hypertension
- x Research into atherosclerosis and the epidemiology of ischaemic heart disease
- x Enzymes in the diagnosis of myocardial infarction

The 1960's:

- x Coronary care units
- x Pacemakers and other electric devices for treatment of arrhythmias
- Valvular prostheses
- x Coronary by-pass operations
- Cardiac transplantation
- x "Preventive cardiology"

The 1970's:

- x Development of noninvasive radiological diagnostic techniques

The heart brought back into the human organism?

— — — — —
 x = of importance for ischaemic heart disease.

Table I

Now fifteen years later, one might use that analysis as a point of departure in judging what progress has been made, what questions have been answered, what new questions have been asked, what action has been taken, where have we got now and where do we go from here?

I believe that such examinations, from time to time, may be useful also as contribution to the study of the proper choice of problems for scientific investigation and the prediction of their relevance - a subject which, a few years ago, I had the privilege to hear Sir Hans Krebs discuss before the Annual meeting of the German Society for Internal Medicine (6).

"Some fundamental problems in coronary heart disease"

In Gustav Nylin's department I had been working with methods to diagnose early - or latent - coronary insufficiency, such as hypoxemia and exercise electrocardiograms. Later on, I had the privilege to study human heart muscle myoglobin and cytochromes under the guidance of two future Nobel Laureates, Hugo Theorell and Christian de Duve, in the hope that the respiratory chain might be crucial to the problems of ischaemia. This, unfortunately, was not to be the case. In the early 1950's, I was given a chance to work with Paul White and Ancel Keys in their international attack on the epidemiology of coronary heart disease, and the set-up in Malmö proved ideal for a comprehensive, hospital-based investigation of ischaemic heart disease in a community.

Neither of these approaches appeared to be particularly useful under the circumstances prevailing in the Seraphimer Hospital at the end of the 1950's. With the acute mortality in patients with myocardial infarction remaining at the 30 per cent level since before World War II, the necessity to "do something" about it was imperative, both as regards the immediate treatment and in the search for pathogenic mechanisms that might render prevention feasible. I have tried to list some of the items which I discussed in my "position" paper, called "Some fundamental problems in coronary heart disease" (5), in Table II.

Problems unsolved fifteen years ago

<u>The delinquent:</u>	<u>The target:</u>	<u>The modifiers:</u>
<u>The coronary artery</u>	<u>The myocardium</u>	<u>Neuro-humoral influences</u>
Atherosclerosis Thrombosis		
<u>The susceptible</u>	<u>The infarct</u>	<u>The arrhythmias</u>
The meaning of "risk factors"	Characteristics of the infarct patient	Studies badly needed of: myocardial metabolism electrical activity new drugs
Genetics vs. Environment	Atherosclerosis vs. Throm- bosis	
Biology vs. Psycho-social		
"The pathogenic situation"	Mortality: <u>Acute</u> 30 per cent	
Mechanisms of environmental fac- tors?	<u>Late</u> 80-90 per cent CVD	
Influence <u>external</u> or <u>internal</u> environment?	Emergency medical treatment - by-pass and homografts?	
(Preventive medicine vs. biochemi- stry and neurophysiology)	Establishing medical-surgical coronary centers?	
"Susceptible" - but at what age?		

Table II

In retrospect, one can state, that all the problems and most of the ways to solve them that we know of to-day, fifteen years later, were known to us already at that time. Yet, most problems remain essentially unsolved. It is surprising to find, how little advance has been made, in theory, over those years, although our ability to develop and assemble gadgets and, thus, make progress in numbers and safety of certain procedures has been remarkable.

A research strategy

In clinical medicine, a research strategy must take into account both the "assault of the immediate empiricism" as William Castle once put it, and the resources in manpower and laboratory outfit at one's disposal. Manpower was a greater asset than laboratory resources, and patients were certainly not a limiting factor in our department of medicine. We therefore, set out to study patients with "heart attacks", following the clues in different directions. On figure 10 I have tried to summarize the areas into which we have gone, or at least dispatched some scouts, during these years. We have done little in the way of conventional epidemiology; neither have we done very much in the lipid business or with regard to coronary surgery. Our policy has been to try to explore areas and problems that were not quite "in" at that time, such as carbohydrate metabolism in relation to ischaemic heart disease, and - in particular - the genetic aspects with regard to both biological and psycho-social factors. We have been fortunate in co-operating over a long time with the large Swedish Twin Registry, operated by the Karolinska Institutet, which has provided us with unique possibilities for clinical twin studies in our department. Of crucial importance to us became the establishment in 1967 of a coronary care unit that lent itself very well also as a research laboratory. Over and above, however, we have tried to follow the advice of that great Regius Professor of Medicine at this University who stated: "If you have the good fortune to command a large clinic, remember that one of your chief duties is the tabulation and analysis of the carefully recorded experience".

ISCHAEMIC HEART DISEASE: PROBLEM AREAS

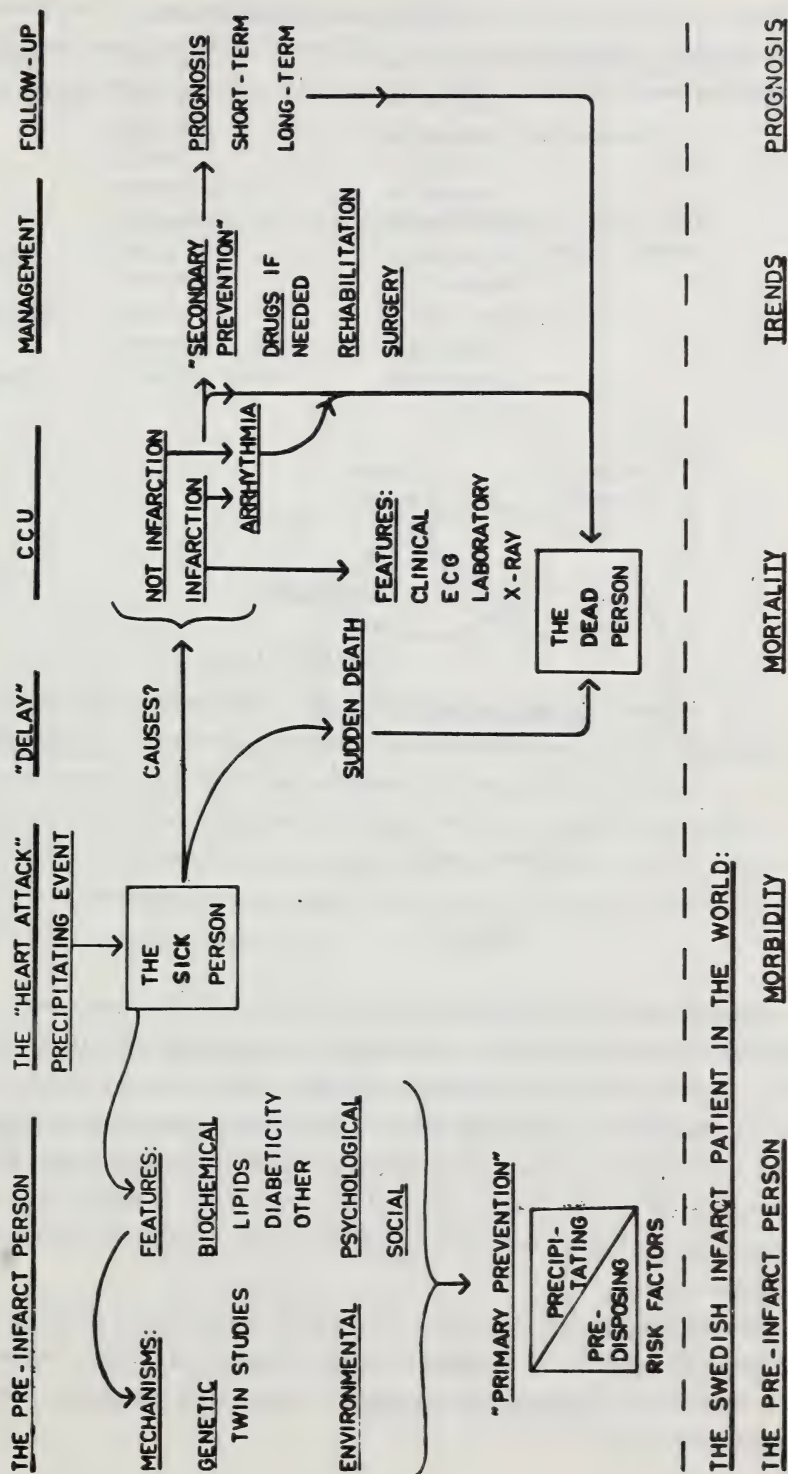


Fig. 10

Now, what are we actually talking about? The label "ischaemic heart disease" comprises several, different clinical manifestations, of whom the main ones are depicted in this Venn-diagram (Fig. 11):

Four sets of clinical manifestations of ischaemic heart disease

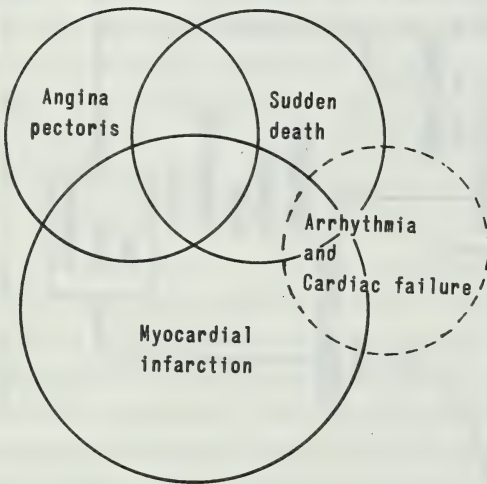


Fig. 11

Some of our patients belong to more than one of the "sets"; others move from one "set" to another in the course of time; still others remain within the same set all the time. The major set at Heberden's time was angina pectoris, but this is perhaps no longer so. The myocardial infarction now seems to be the main item; if one accepts the term "heart attack" you will need a wider circle to describe that set, as it will include also transient arrhythmias and sudden death.

Terminology is not the only difficulty when we are dealing with general aspects of ischaemic heart disease. In fact, there are a number of "contrasting concepts" concerning ischaemic heart disease (Table III):

Contrasting concepts concerning IHD

<u>risk factors</u>	"causes"	or "indices" (or mere "associations")
<u>etiologic factors</u>	"genetic"	or "acquired"
	{ endogenous	or { exogenous (environmental)
	{ internal	{ external
	"psycho-social"	or physical
	predisposing	or precipitating
<u>target organ</u>	artery	or myocardium
	("coronary")	("ischaemic")
<u>natural history</u>	chronic	or acute (sudden death)
<u>impact</u>	morbidity	or mortality
<u>interference</u>	(true) prevention	or postponement

Table III

If we are to deal with the problem of "medical" versus "psycho-social" factors (and I am here, of course, using "medical" in a very restricted "natural science"-sense, while freely admitting that it would be equally, or more, correct to include "psycho-social" elements within the "medical" frame) - then these particular "contrasting concepts" may apply to various levels in the disease process (Table IV).

If, then, we go back to figure 10, one must admit that some problem areas, perhaps the most important, and where the "psycho-social" element might be most decisive, remain largely unknown: Who is the sick person? What precipitated the attack? What did cause the "delay"? Why did some not survive?

"Medical" versus "Psycho-social"Levels:

<u>Predisposing factors</u>	{ The susceptible ("pre-infarct") person Impact of "civilization"	} <u>"Life changes"</u>
<u>Factors affecting prognosis</u>	{ Precipitating events (Anatomy and effects of actual lesion) Delay in seeking help Treatment, immediate and long-term ("secondary prevention")	

Table IVThe clinical reality and the coronary care unit

Even though we at times find ourselves immersed in a sea of "psycho-social" concepts, as clinicians we must always try to establish the hard medical facts to test theories and interpretations. I will, therefore, start my survey in the "forward" direction with the clinical reality.

Assessing the challenges before us, fifteen years ago (5), I observed that there were "few diseases in the field of internal medicine, where the average mortality during 4 to 6 weeks of hospitalization is over 30 per cent". It appeared "necessary that more energy be directed to a considerable reduction of these figures. - Our surgical brethren would never accept a mortality of this magnitude and would certainly mobilize personnel and technique to bring such figures down". To this end, "emergency therapy (should) be instituted at shortest notice and currently

adjusted to the changing situation. This means continuous observation by competent personnel and with the aid of monitoring equipment, particularly with regard to the development of arrhythmias". It took me three more years to get some "monitoring equipment", but we failed completely in getting sufficient nursing staff to watch the screen and had to abandon our attempts. Part of the reason for this was that we simply did not have enough patients with myocardial infarction in the early 1960's to convince the administrators. But in the following years their numbers increased, and the mortality, and we simply felt that something had to be done. In 1967, we borrowed some equipment, set our carpenters and electricians to work and put our administrators before a fait accompli: a coronary care unit with three rooms and a monitor in the corridor. In this unit we could accommodate less than half of the patients admitted with suspected myocardial infarction. One year later, laying our hands on some donations of a hundred years standing, we could establish "some private rooms in a healthy location", which is our present coronary care unit (CCU), with seven acute beds and fourteen "transfer" beds. Here, to date four thousand patients have been cared for, and from this unit seven doctoral theses and many other papers have emerged.

Let me, however, first give you some general background data. During the last fifteen years in my hospital - and it is more or less true for the whole country - the department of medicine has been submerged by a flood of emergency cases, which now make up 80 per cent of all admissions as against 15-20 per cent in earlier years. At the same time, the mean age of those thus admitted has risen by more than ten years, from 54 to 65 years of age.

It looks as if it were the same people who come back, perpetually. They do not die and they do not all become custodial cases. A special study of 200 consecutive pensioners, admitted during one month, and having a mean age of 76, did show that 3/4

got back to their own homes, 5 per cent were transferred to other departments, 10 per cent went to custodial care of the aged and 10 per cent died. This is to a large extent the task of a department of medicine to-day, with regard to care and cure, and there is little likelihood that we will see great changes in these patterns in the near future. (Part of that process can be visualized also in figure 8, dealing with acute myocardial infarction in Malmö). Fig. 12 is an estimate of our present coronary care unit population (page 28).

Claes Helmers, a year ago, made a study of 600 consecutive patients with acute myocardial infarction (AMI) in our CCU (7). Of these, 49 per cent were 67 years old or more, that means: were retired with their "folk-pensions". Over six years we have only had five patients 40 years old or less. Is this at variance with your experience? If so - may it nevertheless be of interest to you? Perhaps - for if you succeed in "prevention" of ischaemic heart disease, which to my mind means "post-ponement" of its clinical manifestations, you may well arrive where we are now.

Another aspect of this problem may well be mentioned. Several years ago, Michael Oliver asked me to collaborate in a European study of "young coronaries", made up by men with an infarct before or at age 40 (8). It took us more than 240 consecutive admissions to get hold of one such person, and he turned out to be a Finn, on a visit to Stockholm. During six years we have admitted only 25 men and one woman aged 45 or less. 14 of the 25 were heavy smokers and only 2 were non-smokers. Such data may indicate that our myocardial infarction "population" is somewhat different from yours.

Estimated course of 1000 patients admitted to our coronary care unit 1968 - 1974.

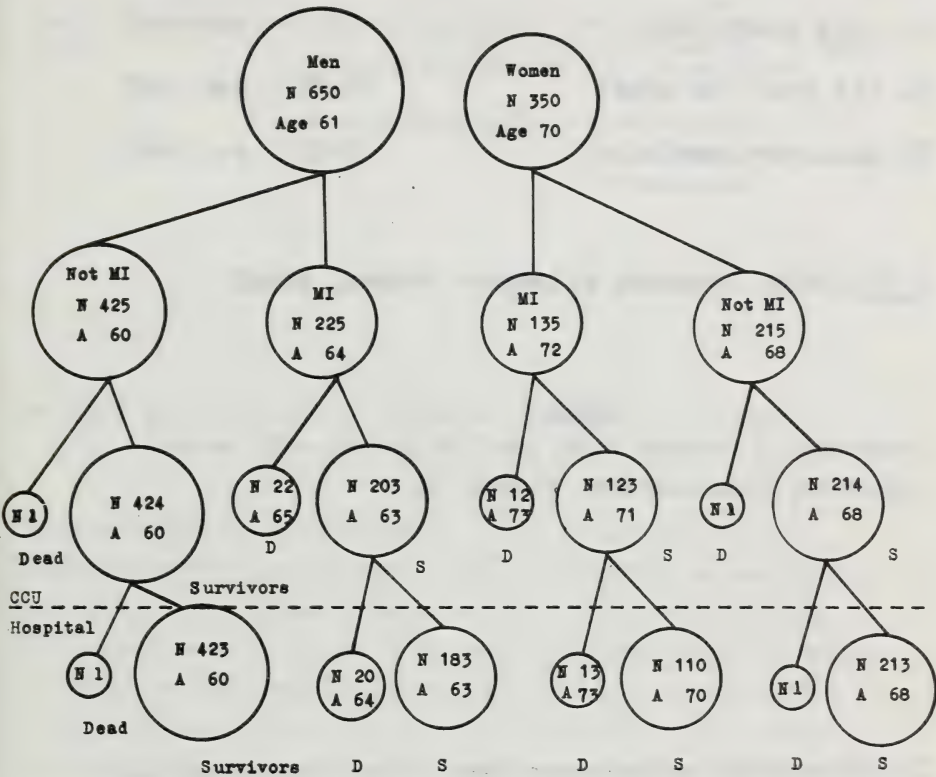


Fig. 12

What have we learnt about the infarct patient?

Of nine average "heart attack" patients admitted to our CCU - in 95 per cent on the basis of "central chest pain" criteria (Table V) - thus, six are men and three are women.

"Central Chest Pain":

1. <u>Only</u> retrosternal	10-15	per cent
2. Retrosternal <u>and</u> precordial	5-6	per cent
3. <u>Only</u> precordial	35	per cent
4. All over the chest	35-40	per cent
5. Non-characteristic	5-10	per cent

A few only: Syncope, pulmonary oedema, shock

Table V

Occurrence of "central chest pain" in patients with acute myocardial infarction acc. to Säwe (9).

Two men aged 64, and one woman, aged 72, were having AMI, while four men and two women did not meet the diagnostic criteria for AMI; these were four years younger than the infarct patients. Yet, they had "central chest pain" to the same extent as the "infarcts" but less "radiation of pain". In contrast to the infarct patients, this group carried an almost negligible short-term mortality. The infarct mortality was about 10 per cent in the CCU and another 10 per cent during the rest of the hospital stay.

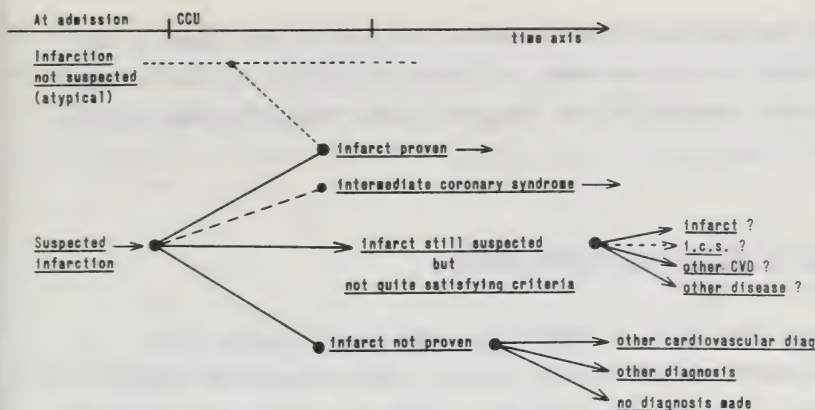


Fig. 13

Flow chart for patients with suspected myocardial infarction.

Urbain Säwe has also studied a group of patients with an "intermediate coronary syndrome" (Fig. 13), defined as having an increase of S-GOT values by more than 10 units - though within the "normal" range - within 24-48 hours from the onset of symptoms (10). Such patients made up 10 per cent of all those admitted to our CCU (corresponding to 20 per cent of the true AMI:s). Their long-term prognosis is now being studied. As for the "infarcts that were not", many of whom may have ischaemic heart disease, we are likewise now analyzing what has become of them.

I have not here otherwise dealt with angina pectoris. Frankly, we do not see very much severe, or intractable, angina. A reduction may have been obtained by the use of β -blockers, but I doubt that this accounts for very much. Candidates for coronary surgery have, thus, been few in Sweden, as intractable angina - and possible preinfarction angina - have been our main indications for surgery. By-pass operations in Sweden, (where thoracic surgery has long been a prominent speciality,) have not numbered more than perhaps two hundred in five years time. In the Stockholm region,

professor Viking Olov Björk believes that one or two cases a week will be done in years to come. It is worth mentioning that a fair number of the candidates, so far, have been younger Finns, working in Sweden (11).

The dangerous delay and sudden death

In more than half of "medically unattended" deaths from ischaemic heart disease in our country, the subjects die within 15 minutes of the onset of symptoms. Very few manage to appeal for efficient help. Obviously, the "delay" mechanisms in such instances are extremely strong. Sudden death makes up 40 per cent of our male and 20 per cent of our female ischaemic heart disease deaths.

A study of the various delay fractions for patients arriving in our CCU (12) showed that only one third of the patients with central chest pain did call for help within the first half hour, while as many waited for 3 hours or more. The patients' sex, age or self-diagnosis did not affect this delay, while previous CCU-care and/or visit to a physician during the last year, as well as "not being at home at the time" did shorten it. Of crucial importance seems to be the patient's personal "decision time". It would be interesting to subject this factor to a thorough psychological penetration, to identify the various, rational and irrational, arguments that are involved. Attention to an intriguing malaise in combination with weakness and pain may conceivably induce restraint and withdrawal rather than outward activity.

Our data indicate that sensible decisions are more easily made by others than by the patient himself. Nevertheless, probably no more than 25 per cent of those developing truly malignant arrhythmias might possibly be brought under proper care within such time limits that the condition is still manageable and reversible (12).

In 75 per cent of Wiklund's (13) material of medically unattended deaths, earlier ischaemic heart disease was known or could be suspected. Romo (14), in Finland, could not find useful criteria to predict the occurrence of 240 sudden deaths in a total

material of 1.270 heart attacks in persons below age 65. In our material (15), apart from more than one previous infarct, angina of recent origin and ventricular tachycardia during the first CCU day seem to carry an increased risk for a future sudden death.

Causes of death

The main usefulness of the CCU is in the prevention of so-called "electrical death" from malignant arrhythmias. Our first, provisional CCU, with only 3 beds, and meeting only half the real demand, gave us an opportunity to study the effects of a forced random allocation of infarct patients to the CCU and the ordinary wards. Stefan Hofvendahl (16) was able to show that patients in the general wards continued to have a 35 per cent four week hospital mortality, whereas the mortality of the CCU-patients was 17 per cent, half of which occurred after the transfer to a general ward. In our total material, as shown earlier, the latter figures are of the same order. The dividends of the CCU seem to have reached a steady level with little prospect of any dramatic, future improvement. There are obvious limits to what can be done, if too large a muscle mass is destroyed, or the papillary muscles are severely damaged ("pump failure"). Such facts set the limit for success with counter-pulsation techniques (17) or even heroic surgery within or outside the CCU (18-20). The "clinical" causes of death (7) in our CCU and after transfer to general wards were as shown in Table VI.

Behind these "causes" the pathologist will find another set of causes. It should not be forgotten, that hospital patients die of myocardial infarction also outside the CCU.

Mode of death in 400 patients, 1968-1969

	<u>CCU</u>		<u>Hospital</u>
	<u>Day 1</u>	<u>Later</u>	<u>After-care</u>
Primary electric failure	1		4
Secondary electric failure	4	4	18
Shock	10	12	4
Pulmonary oedema	5	3	8
Shock and pulmonary oedema	2	2	
Cardiac rupture	5	3	1
Other causes		1	2
Total (N = 89)	27	25	37

Table VI

Mona Britton (21), in a thesis evaluating the impact and importance of autopsies, showed that in some few cases pulmonary embolism, rupture of the aorta, severe aortic stenosis or acute haemorrhagic pancreatitis had produced symptoms and signs compatible with a diagnosis of myocardial infarction, chiefly in elderly patients. On the other hand, recent myocardial infarcts were found in fifteen out of fifty patients witout a previous history of ischaemic heart disease, and either dying shortly after arrival in the hospital, or suddenly, while being hospitalized for other conditions, and in whom the cause of death, clinically, was considered as "unknown".

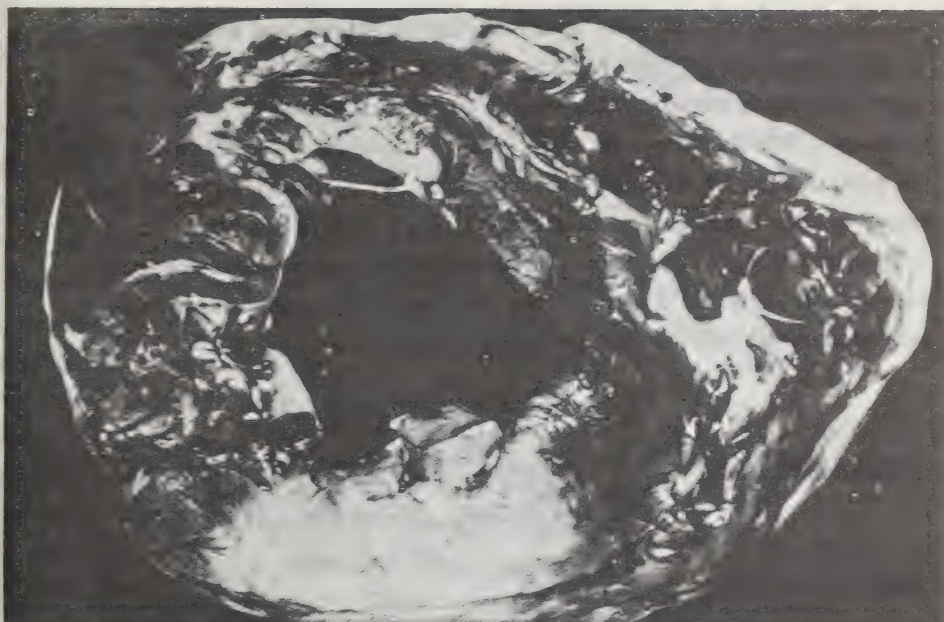


Fig. 14 A

Transmural infarct, acc. to Erhardt (22).

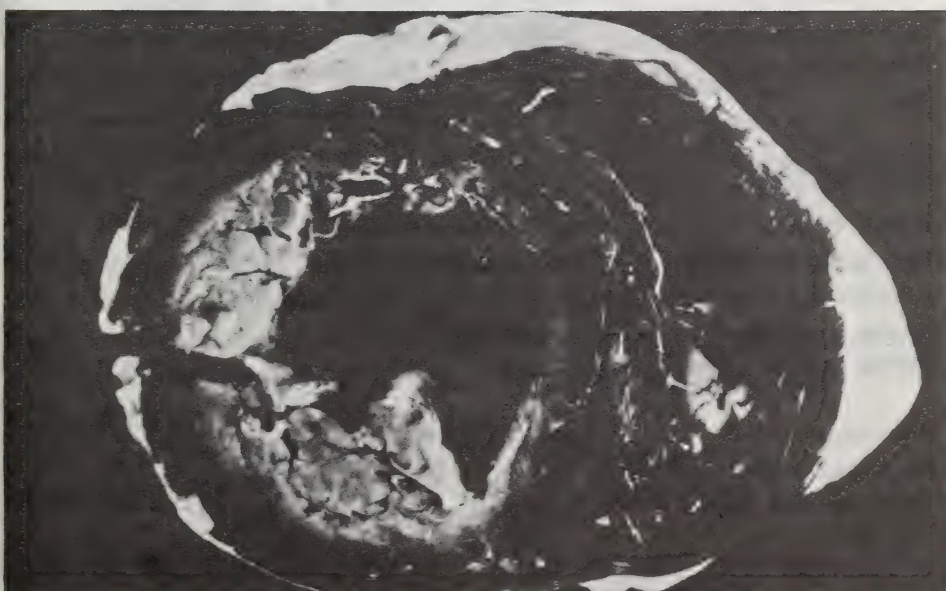


Fig. 14 B

Subendocardial infarct., acc. to Erhardt (22).

Leif Erhardt (22) has analyzed the clinical and pathoanatomical significance of different types of myocardial infarcts, such as they are encountered to-day among the fatal cases in a coronary care unit (Table VII) - a task similar to that undertaken earlier here at Oxford by Mitchell and Schwartz. In 84 detailed autopsies using enzyme staining on transverse heart slices he found a transmural infarction (Fig. 14 A) in 58 per cent, subendocardial infarction (Fig. 14 B) in 19 per cent and combined transmural-subendocardial ones in 23 per cent of the cases.

<u>TYPE OF INFORMATION</u>	<u>TYPE OF INFARCT</u>		
	<u>TRANSMURAL</u>	<u>COMBINED</u>	<u>SUBENDOCARDIAL</u>
	58 PER CENT	23 PER CENT	19 PER CENT

ANATOMY

CORONARY THROMBOSIS	<u>FREQUENT</u>	<u>FREQUENT</u>	<u>INFREQUENT</u>
VARYING AGE OF NECROSIS	<u>INFREQUENT</u>	MOD. FREQUENT	<u>FREQUENT</u>
MYOCARDIAL FIBROSIS	MODERATE	EXTENSIVE	<u>VERY EXTENSIVE</u>
RUPTURE OF L.V.	<u>FREQUENT</u>	RARE	<u>ABSENT</u>
MURAL THROMBI L.V.	<u>FREQUENT</u>	MOD. FREQUENT	<u>INFREQUENT</u>
SIZE	LARGE	<u>VERY LARGE</u>	<u>SMALL</u>

CLINICAL FEATURES

HISTORY OF ANGINA	MOD. FREQUENT	FREQUENT	<u>VERY FREQUENT</u>
<u>PRECIPITATED BY STRESS</u> (PHYSICAL OR EMOTIONAL)	MOD. FREQUENT	INFREQUENT	<u>ABSENT</u>
<u>AUTONOMIC SYMPTOMS</u>	<u>VERY FREQUENT</u>	FREQUENT	MOD. FREQUENT
<u>ARRIVAL IN CCU < 4 HOURS</u>	FREQUENT	MOD. FREQUENT	<u>INFREQUENT</u>
HYPOTENSION OR SHOCK	VERY FREQUENT	VERY FREQUENT	<u>INFREQUENT</u>
NON-DIAGNOSTIC ECG	RARE	INFREQUENT	<u>FREQUENT</u>
SUDDEN DEATH IN HOSPITAL	INFREQUENT	INFREQUENT	<u>FREQUENT</u>

There were no significant differences in mean age between these three groups - the average patient being 70 years old.

Coronary thrombosis was very frequently found in the transmural and combined infarcts (84 %), but infrequently (25 %) in the subendocardial ones. A varying age of the myocardial necrosis and a high degree of myocardial fibrosis was found more frequently in the subendocardial infarcts. Clinically, such patients had a longer history of angina pectoris; their infarct was less often preceded by physical exertion or emotional stress than in the transmural cases; they were late arrivers in the CCU, with fewer "autonomic" symptoms and less hypotension or shock. Their electrocardiogram was more often non-diagnostic than in the transmural cases, displaying only ST-depression, yet they were the very patients who died suddenly and unexpectedly during the hospital course in contrast to the transmural cases.

Of the latter patients, 20 per cent in this series instead died from rupture and pericardial tamponade. To my mind, such detailed correlations of structure and dysfunction eventually will give us information regarding the local prerequisites for the infarction process as well as a better insight in the pathophysiological mechanisms involved. Do different etiological mechanisms lead to different courses with regard to pathology and clinical manifestations (Fig. 15)?

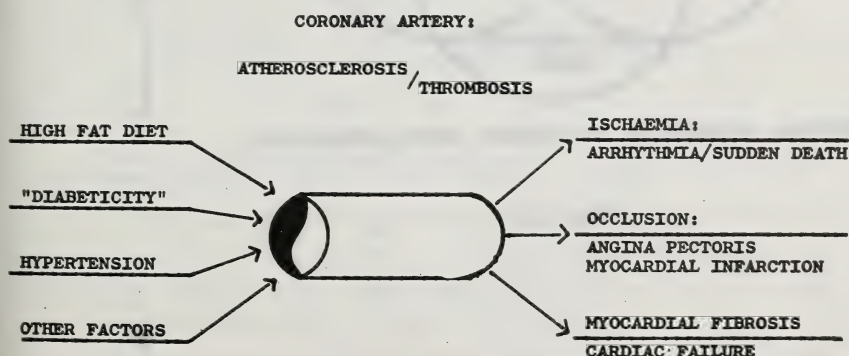


Fig. 15

A crucial element here is, of course, the old question of the role of the coronary thrombosis: Whether cause or consequence of the infarct? Erhardt and co-workers (23) have also tried to contribute a partial answer to the question by injections of radioactively labelled material, which was later found to be included in coronary thrombi in fatal cases. At least in some cases, the thrombus seems to develop after the clinical signs and symptoms of a myocardial infarction have occurred. The extension of such studies is obviously very important, for we are still very much in the dark as to the time-course of the infarct evolution (24), and unless this problem is clarified, our hypotheses concerning possible precipitating factors remain mere speculations.

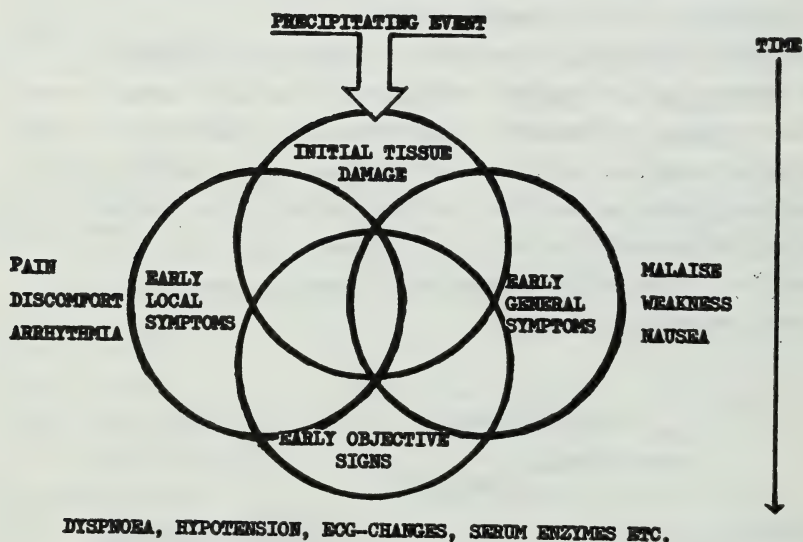


Fig. 16

But in an ever wider context, the problem of a primary myocardial and/or neurohormonal cause of heart muscle necrosis in certain situations will have to be examined. The terms "ischaemia" and "coronary" heart disease have long been considered synonymous,

the former being English and the latter American. They may, however, well cover two different patho-physiological concepts and realities.

Dysrhythmias

In this connection, words about malignant dysrhythmias, whether as a spin-off from an infarction process, or as an independent disorder. Here, the concept "ischaemic" may be much more relevant than "coronary". We know, that both tachycardia and ectopic beats are very frequent in situations of general nervous excitement. Walter Somerville (25) has shown it in drivers and public speakers, and we have registered similar findings in our healthy young colleagues, telemetered during the defence of their academic theses (Fig. 17):

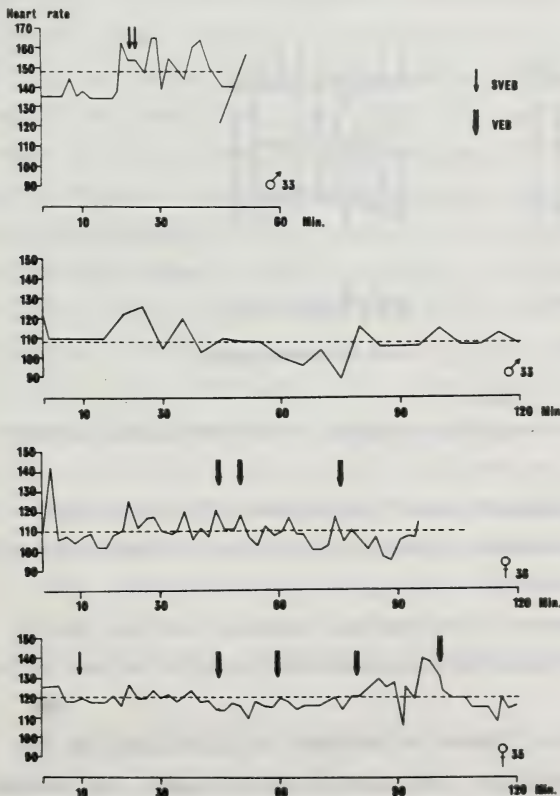


Fig. 17

Heart rate and incidence of ectopic beats in four physicians defending their doctoral theses in public.

Theorell (26) has elicited potentially dangerous runs of ectopic beats in interviews dealing with a person's work situation:

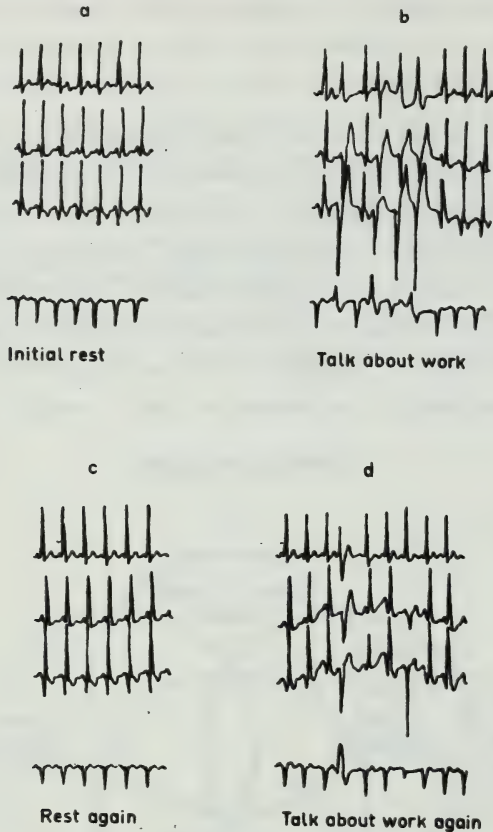


Fig. 18

Electrocardiographic recordings during interview with a patient (26).

In this area it appears that "psycho-social" influences, through the central nervous system, are playing an important role. Yet, once there is structural damage to the myocardium, and particularly in response to myocardial weakness and peripheral regulatory reflexes, obstinate, malignant dysrhythmias may easily develop.

Dysrhythmias were a favourite subject in cardiology in the early times of sphygmography and electrocardiography, but became less fashionable during the many years of electrophysiological theories of depolarization, repolarization and injury currents.

With the realization of the magnitude of the contribution of sudden death to the mortality from ischaemic heart disease and with the technological advances for monitoring and taperecording of cardiac activity over long periods of time, the arrhythmias came very much back into focus and again became fashionable.

Lars Mogensen (27), in a study of the effects of lidocain on dysrhythmias and clinical course of patients with acute myocardial infarction, analyzed 500 kilometers of continuous electrocardiographic tracings from our coronary care unit. He found disturbances of rate, rhythms or conduction in 96 per cent of the patients. Ventricular tachycardia occurred in 40 per cent, primary ventricular fibrillation in 4 per cent. Eight per cent developed AV block III, and seven per cent of the patients had ventricular standstill. Observations in patients who developed their infarct at the CCU have shown that bradyarrhythmias sometimes occur as an early event (28, 29). The variety of dysrhythmias often occurring in one and the same patient, both in myocardial infarction and in other capricious conditions, like the "sick sinus syndrome", have so far made it difficult to extend prophylactic treatment schedules with anti-arrhythmic drugs beyond the hospital walls in patients with tachy-arrhythmias. On the contrary, sixteen years experience with cardiac pace-makers in our department, under the supervision of Olof Edhag (30), and now comprising some seven hundred patients, has proven the tremendous value of such treatment for the many patients with brady-arrhythmias in the community. Pace-makers are given to more than five times as many people per million inhabitants in Sweden as in England, probably in part because of different age distribution in upper age groups between our countries. Every new CCU provides a fair share of pace-maker candidates.

Why did some not survive ? Prognosis and prediction

Can death be predicted? This question has two answers. One refers to death in connection with a first "heart attack", whatever that may signify; the other with the death of those who have survived their first myocardial infarction.

Claes Helmers (7) in his analysis of the deaths in 600 infarct

patients from our CCU, tried to establish "prognostic indices" for the first day, the hospital period and the long term survival, i.e. 3 years, so far.

Such indices are useful not only as guidelines to so-called "informed guessing", but may serve a useful purpose also in assigning priorities for admission to coronary care units with too narrow bed capacity. By means of so-called stepwise linear regression analysis Helmers could show, in both retro- and prospective studies, that useful prognostic indices could be based on quite simple data.

Nyquist (17) had already found systolic blood pressure and respiratory rate on admission to be predictive of development of shock later on. Helmers found that age and respiratory rate on admission were the main factors indicating total first-day prognosis; respiratory rate on admission and maximum S-GOT were most useful in predicting prognosis during the remainder of the hospital stay, and age together with the maximum respiratory rate during the CCU stay and the presence of left bundle branch block gave the best clues as to the three-year survival rates (7).

Studies from Gothenburg (31) appear to confirm this impression in as much as dyspnea in connection with the acute attack, and S-GOT values, appeared to have a high long-term prognostic significance in myocardial infarction.

The importance of "pump failure" as contrasted to "electrical failure" should, however, not be underestimated. In the early 1960's, before the full impact of the electrical instability had been revealed by oscilloscopic monitoring, we directed our interest toward the study of pump-failure, acute and chronic, in patients with myocardial infarction in order to assess the value of digitalization in such conditions. Robert O. Malmberg (32) devoted his thesis work to this problem, but in the absence of CCU facilities at that time, the management and elucidation of the acute situation met with great difficulties. Later on, within the setting of the CCU, Andreas Sjögren (33) made a thorough study of left heart failure in acute myocardial infarction: such patients were generally older, had larger infarcts and developed more severe arterial hypoxaemia. Ouabain was of very moderate usefulness in

such cases; however, a potent diuretic such as frusemide gave a more prompt and dramatic effect. Sjögren also could show that the pulmonary artery diastolic pressure was closely correlated to other expressions of the severity of the left heart failure and to the prognosis; the most reliable and convenient indication of the PADp turned out to be the amount of pulmonary rales at auscultation. Chest X-ray was less helpful in this respect.

It is remarkable, how important simple respiratory data seem to be as indicators. Great attention is, therefore, being paid to auscultation of the lungs and counting of respiratory rate in our coronary care unit.

A crucial question is, of course, how lasting the gains of the coronary care have shown themselves to be. Are they only temporary, or are they lasting? Are they worth while? The survival after discharge from our first CCU has now been followed for more than five years (34). The gains in survival rate for the original CCU group mentioned earlier (16) were maintained over these years (Fig. 19).

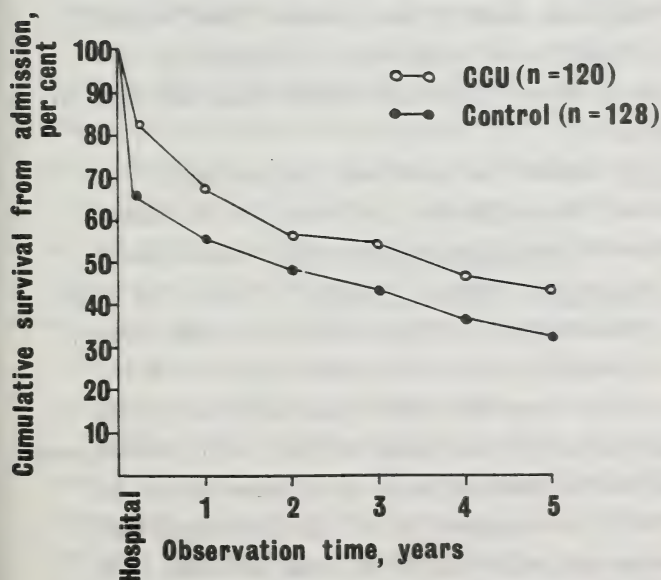


Fig. 19

Who was the pre-infarct person?

If by now we return to the left part of figure 10, we may consider the pre-infarct person. Who was the pre-infarct person, whom we have met in the CCU, and who is the susceptible, pre-infarct person, in this room, who - with or without his own knowledge - is thought of as being doomed, sooner or later, to suffer a heart attack?

It is hard to know, in retrospect, who the infarct patient was. With regard both to biological factors (particularly biochemical), and to "psycho-social" ones, the infarct and what it means may have elicited profound changes in the patient. In studies of the histo-chemistry of the infarct heart - as we have been doing with regard to respiratory enzymes and trace elements (35) - one can never avoid the question: cause or effect? But also general metabolic features may change, at least temporarily.

Through a combination of prospective and retrospective data it has been possible to identify a number of factors that characterize the pre-infarct person and tell us who the pre-infarct person is. They have usually been called "risk factors". Personally I prefer to call them "indices", biological or psychological, because I do not think one should jump too fast in making inferences here.

Of the biochemical factors, we have been particularly interested in two. Kjell Hellström and his group (36-38) have studied the metabolism of hyperlipoproteinaemias, particularly with regard to the intestinal feed-back control of the bile acid synthesis, which is instrumental in the elimination, and thereby the regulation, of cholesterol. In Fredrickson's type II A the elimination of cholesterol does not differ quantitatively from normal, but the proportion of cholic acid is low. With cholestyramin this returns towards normal. There appears to be some defect in the programming of the liver enzymes, or of the intestinal re-absorption. The inverse situation exists in some patients with type IV, where the production and elimination of cholic acid is in a high gear. This contributes to a greater cholesterol elimination. It is perhaps of interest that in our material there is a male

predominance of type IV patients, while more females belong to type II A.

It is obvious that we must know more about the feed-back mechanisms that regulate the synthesis and elimination of cholesterol metabolites, which ultimately can be recognized in the plasma levels of cholesterol - a yardstick with which clinicians (and patients!), right or wrong, measure the severity of disease and the success of treatment. The secrets of atherosclerosis may eventually be discovered in the liver and the gut, thus bringing cardiology and gastroenterology to meet within internal medicine-at-large.

During my years in Malmö, we had collected a fair amount of epidemiological data on ischaemic heart disease in a "captive" one town - one hospital population. Among the important observations was the high prevalence of diabetes among the infarct patients in relation to that in the population-at-large. At the Seraphimer hospital, Fredrik Wahlberg (39) initiated a study of the intravenous glucose tolerance in patients without overt diabetes but with ischaemic heart disease as manifested by a previous myocardial infarction, or angina pectoris or intermittent claudication. He found a remarkably high incidence of low glucose tolerance ("latent diabetes") in such patients as compared to controls, and he could also show that patients with a low glucose tolerance had a poorer long-term prognosis than those with normal values. This observation has now been confirmed in a 10-year follow-up (40). Together with Lars A. Carlson he could also show that there was no constant relationship between glucose tolerance and hyperlipidemia. This was before the more sophisticated classifications of lipid abnormalities had been developed, and it was concluded that "diabeticity" per se could be a risk factor, which might be amenable to prophylactic management.

Such a study was therefore started, and the results of a 4 1/2-year follow-up study of 178 survivors from a first myocardial infarction without overt diabetes, half of whom were put on an ambulant tolbutamide treatment, while the other half received placebo, were reported by Juhani Paasikivi (41) in 1970. The tolbutamide-treated patients showed a significantly improved survival during the first 18 months, and this was particularly

true of those with abnormal glucose tolerance, in whom the glucose tolerance also improved for the whole period under study, A reduction in serum triglycerides was also observed. A high risk group with signs of heart failure appeared to benefit most from the treatment.

While it is too early to draw far-reaching conclusions from such studies, a closer look into the relationship of impaired glucose tolerance and particularly type IV hyperlipoproteinaemia would probably be rewarding.

Parallel to the research on factors connected with the atherosclerosis, reconnaissance into areas of thrombogenesis (42-44) and of the biochemistry of human heart muscle has also been tried. While I returned to my old favourites, cytochrome c and myoglobin, in the hope of finding some loose end to pull with regard to the respiratory chain and oxygen store in ischaemia (45-47), Per-Ola Wester made an all-out attack on trace elements in the myocardium by means of neutron activation techniques (35), thereby producing a map of 25 trace elements under various clinical conditions. Like in most other - and later - trace element studies, reviewed by the WHO, the data as yet seem too scattered to provide a truly meaningful picture. But the lasting challenge from the hard water-mystery (48-50) will, no doubt, necessitate a deeper plunge into the trace element pool, in order to establish a meaningful connection between our heart and that part of our environment.

Most risk factors established so far, are "medical". Yet it is in the make-up of the pre-infarct person and in the impact of "our civilization", to quote WHO, that psycho-social factors have been assigned the greatest importance. Despite the ambiguity of the WHO - which in one document recommends the governments to "change the modern way of living as such" (2) and in another feels that "no relation has been found between personality traits and the risk factor score" whence "psychological factors should not be given prominence in prevention trials" (51) - we have attempted to study precisely such factors.

Predisposing and precipitating factors

In such endeavours we have felt it mandatory to work with two concepts in the analysis of the pre-infarct situation, viz. pre-disposing and precipitating factors (Fig. 20).

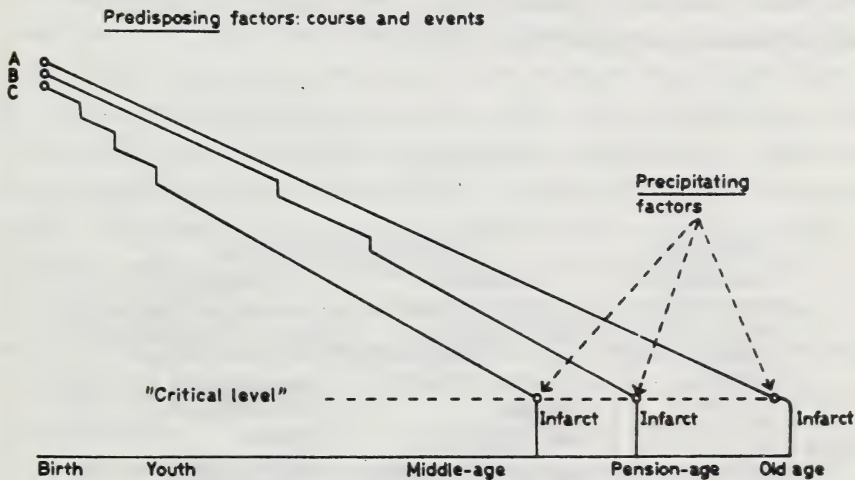


Fig. 20

A, B and C represent persons, or groups, who "lose potential" at different rates and, therefore, arrive at a critical level at different times.

Predisposing factors may, in principle, be genetically determined. These are the ones that set the biological clock-work of the individual and determine the consumption of this endowed life-potential. This may happen gradually, or stepwise. Precipitating factors are those that elicit major, decisive changes in the normal physiology, causing serious disease or death. They may strike like a lightning, or may occur in the form of a gradual build-up of charges ("life changes"). They originate in the environment and

its demands on the individual, or - to put it the other way - in the individual's wrestling with an unyielding environment, (here taken in a wider sense of the word). To this category belongs the "maladaptation to our civilization", in WHO:s words.

Theorell, Rahe, Liljefors, Lind in our department and Birgitta Flodérus, a sociologist in the department of Environmental Hygiene, have been working with these problems using different approaches (52-60).

The main findings in these, rather intricate, studies may perhaps be summarized thus (Table VIII):

		<u>Risk factors</u>		<u>Myocardial infarction (IHD)</u>	
		PROSPECTIVE		RETROSPECTIVE	PROSPECTIVE
Predisposing		High <u>neuroticism</u> correlating with alcohol ⁺ cigarettes ⁺ diast. bl.pr. ⁺ chol. + TG ⁺ phys. act. ⁺ ----- "Self-made": syst. bl.pr. ⁺ smoking ⁺		Twins with <u>more</u> IHD: <u>more</u> life dissatisfaction <u>more</u> devotion to work MI-patients: <u>lower</u> education re. responsibility <u>more</u> early life <u>conflicts</u> <u>more</u> changes of residence <u>more</u> overtime work <u>less</u> social activities <u>more</u> life dissatisfaction	Twins with <u>more</u> problems at work or in family <u>more</u> new angina and <u>more</u> sudden death Screening: High psychosocial "Discord index" indicates <u>increased risk</u> of suffering MI or SD next year (not other diseases).
	Precipitating	—		MI-patients: <u>more</u> <u>life changes</u> last $\frac{1}{2}$ year <u>more</u> <u>change of work situation</u> <u>more</u> <u>upset</u> by this	MI-patients: "stress-interviews" elicit potentially <u>dangerous arrhythmias</u> Catecholamines correlate with "life changes".

Table VIII

Many of the well-known predisposing "risk factors", such as elevated blood pressure, elevated serum lipids, excessive cigarette smoking and alcohol consumption together with low

physical activity belong to a cluster which also comprises "nervousness", restlessness, sleep disturbances, strong pre-occupation with work, overtime, discontent and personal conflicts. The psychologist's interpretation (according to Eysenck) of this is a lack of stability that the person in question tries to reduce by "behavioural coping" by various means, which if intensified, repeated or prolonged may lead to manifest disease and death. If this is true, the relevance of many "risk factors" to the development of ischaemic heart disease is a spurious one, and the term "indices" may be more warranted. Attempts at correction of individual factors may then fail, in as much as they do not aim at the underlying mechanisms. At the same time it should be stressed that some "risk factors" are not specific predictors of ischaemic heart disease but of a generally poor somatic prognosis, "biological aging" as it were. This is in accordance with the findings from our twin studies, where Lundman and his co-workers have found cigarette smoking to be correlated to drinking, and the higher mortality in smoking twins as against the nonsmoking ones largely to be due to lung cancer, ischaemic heart disease and accidents and suicides.

Flodérus' studies deal with qualities associated with, and possibly predisposing for, ischaemic heart disease. As mentioned before, there may be other factors that precipitate the acute event, in particular a myocardial infarction. This, in turn, has been the subject of a thesis (52) and several subsequent papers by Töres Theorell (56-59). In his studies, Theorell has adhered to the concept of research in psycho-somatic medicine, which may properly be ascribed to Harold G. Wolff. Thus, in his thesis, he analysed the patients psycho-social status with respect to challenges from life situations and compared this information with laboratory data, such as determinations of serum lipids and uric acid and urinary epinephrine. He also made experiments with epinephrine loading under standardized conditions. Both serum triglycerides and uric acid did show variations related to the activity of the adrenomedullary system, while cholesterol was found to be more stable. The daily urinary epinephrine excretion showed an "acceptable" agreement with the amount of weekly "life changes",

as classified in accordance with a technique developed by Holmes and Rahe. Theorell could demonstrate that there was a build-up of serious "life changes" several months before the acute event in many of his cases, and he has devoted much of his subsequent work to the refinement of these studies in order to arrive at a better understanding of why and when a subject enters the risk zone of precipitation of an acute "heart attack". In later studies, Theorell and Lind (58) found systolic blood pressure and cigarette smoking to correlate with some psycho-social variables, viz., discrepancy between social groups and educational level, the "self-made" man having higher blood pressure, whereas cigarette smoking co-varied with reports of conflicts with teachers during school years. No similar correlations were found with cholesterol. Such findings do not, of course, exclude the immediate effects of a variety of physical precipitating factors, alongside with such as "operate through the mind", to use a phrase coined by Sir George Pickering - at day time, or during the night, in our dreams.

Mechanisms: genetic and "environmental"

Behind the "features" of the pre-infarct person, to the extreme left in figure 10, are the "mechanisms". These essentially concern the fundamental questions of heritage and environment and the interplay between both. Practically all "epidemiological" studies of ischaemic heart disease are based upon the concept that such disease is caused by - or at least associated with - environmental factors, which, if properly identified, can be dealt with so as to "prevent" the development of disease. Epidemiological studies over the last twenty years have propagated themselves in a truly epidemic way all over the world. Few studies have concerned themselves with the other facet: the genetic factors. This is so for two reasons: such studies are more difficult to perform and their results, if they do show a strong impact of heredity, are less encouraging for the optimistic, progressive and radical mind. Nevertheless, such studies have to be performed, and have been

performed in our department in collaboration with the Swedish Twin registry.

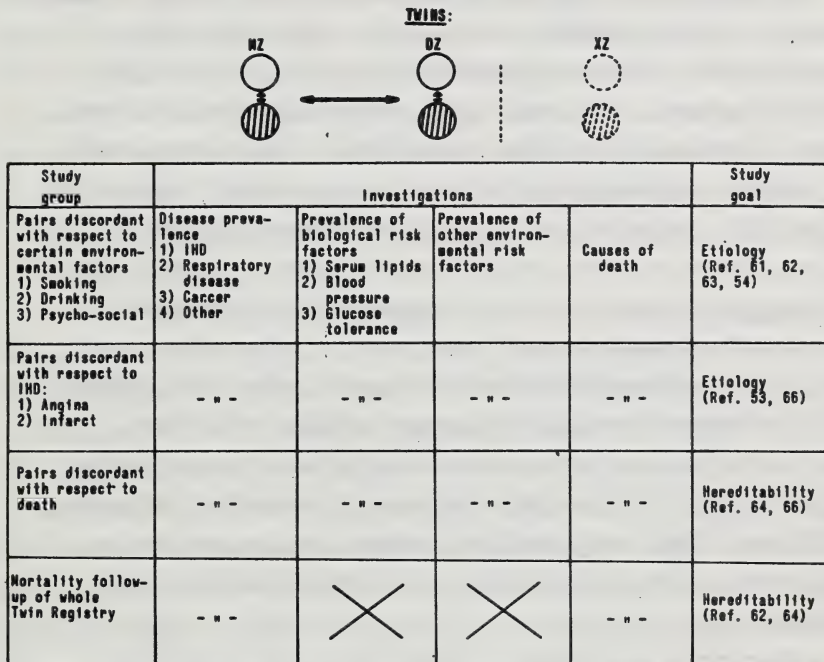


Fig. 21

Investigations into the genetics of ischaemic heart disease.

I shall not go into the technicalities of this type of work, which is based in part on calculations of differences between monozygotic and dizygotic twins, but I will mention the problems that have so far been attacked by us (Fig 21). In a way, they represent a part of the search for figures with regard to the

relative weight of genetic factors in cardiovascular disease, which Sir Georg Pickering asked for in his work on hypertension twenty years ago.

The aims of our first twin study was to examine the alleged relationship between cigarette smoking and ischaemic heart disease. This was done by Torbjörn Lundman (61), and he found no excess morbidity from overt or latent coronary heart disease in the smoking as compared to the non-smoking twins, while there were clear differences between the groups with regard to lung function and respiratory symptoms. (The statistical analysis further indicated that genetic factors did manifest themselves in the electrocardiographic response to exercise.) The question was raised, whether the excess morbidity and mortality from ischaemic heart disease in smokers reported in epidemiological studies might be largely due to constitutional differences between smokers and non-smokers.

Later studies have supported these results, also with regard to mortality in smoking-discordant monozygotic twins (62). There was also a pronounced association between smoking habits and registration for misconduct in the national alcohol registry, and a higher mortality for those thus registered, regardless of smoking habits. It was, then, concluded that smokers and non-smokers are "self-selected" groups, who differ in many other respects than that of smoking.

In another study of male twins 45-65 years old, Myrhed (63) could confirm the association between smoking and drinking, and found high alcohol consumption to be associated with more hypertension, high fasting blood sugar value and impaired glucose tolerance as well as elevated serum uric acid values. There were also more subjective heart symptoms, such as palpitation and irregular heart action in the high alcohol group, but no differences with regard to serum lipids.

In a recent study by de Faire (64), 200 surviving twins below age 70 and with a mean age of 61 were subjected to a thorough clinical examination within five months of the death of the partner. Both male and female co-twins, whose partner had died from ischaemic heart disease, showed signs of such disease more often than those whose partners had died from other causes. An analysis of all the parameters studied indicated that there must be a substantial genetic influence in the development of ischaemic heart disease. This influence is partly mediated through a higher blood pressure in women, whereas in men factors that reflect the mode of living seem to interfere to a greater extent with the genetic influence, an observation earlier made by Harvald and Hauge (65). Such factors, however, did not discriminate between the deceased twin and the survivor.

In the three studies mentioned (61, 63, 64) signs, symptoms and risk factors suggesting ischaemic heart disease were sought for in twin populations, discordant with regard to smoking, alcohol consumption or death (from all causes). Ingvar Liljefors (53), on the contrary, examined a hundred male twin pairs, aged 42-67 years, in whom one or both had reported manifestations of ischaemic heart disease such as previous myocardial infarction, angina pectoris and/or abnormal electrocardiogram. These subjects were then examined both clinically and with regard to so-called psycho-social factors. It was found that ischaemic heart disease was present more often in both of the monozygotic twins than in the dizygotic ones. Apart from diastolic blood pressure, none of the conventional risk factors - not even smoking - differed significantly between the affected and the non-affected twin, while more ambition and overtime work and less physical activity during leisure time was found to characterize the twin with ischaemic heart disease. These findings were further supported in a later study by Liljefors and Rahe.

Recently, Liljefors (66) was able to report from a 7 years follow-up of 36 originally ischaemic heart disease-discordant twins. 10 previously symptom-free partners had now developed ischaemic heart disease. There were no differences with regard to standard risk factors (blood pressure, cholesterol, cigarettes) between those who had and those who had not developed disease manifestations.

In this connection, it may be of interest to mention that Aro in a recent thesis from Helsinki (67) found that familial aggregation of hyperlipoproteinaemias occurred in only 1/3 of first degree relatives of 100 survivors of myocardial infarction under 50 years of age. Electrocardiographic changes suggesting ischaemic heart disease and a family history of myocardial infarction prior to age 65 were not correlated to the aggregation of hyperlipoproteinaemia in the families.

Some inferences seem warranted from these studies:

1. Genetic factors exert an important influence on the development of ischaemic heart disease.
2. This influence appears to be more clearly expressed in women than in men, perhaps because triggering "environmental" factors are more forceful in "the male society".
3. Some conventionally established "risk factors", such as cigarette smoking, may merely be indicators of deeper personality traits, which may express themselves also in other respects, e.g. by high alcohol consumption, accident proneness, depression etc. on the one hand, while - on the other hand - they may be associated with certain "psycho-social" features, labelled "dedication to work", "Type A-personality", "the Sisyphus complex" and so forth.

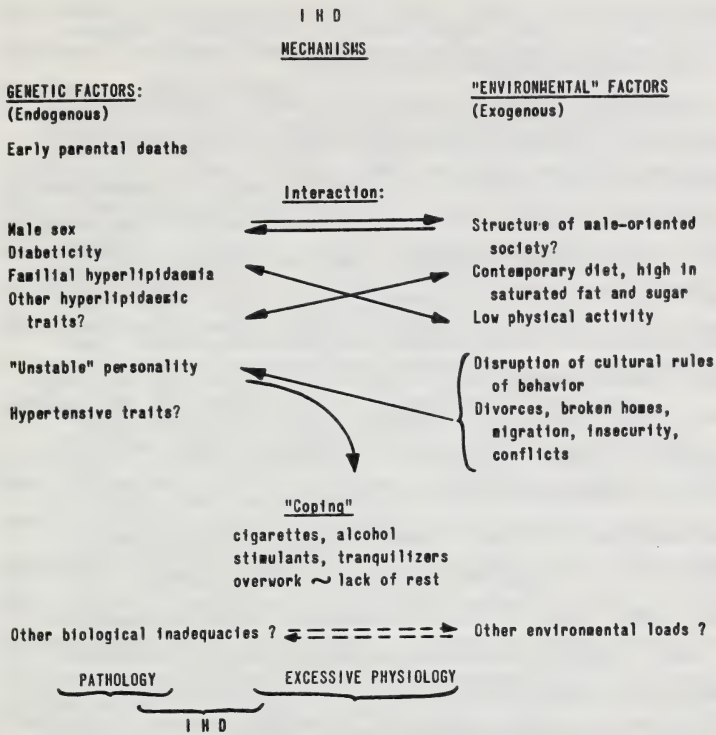


Fig. 22

An attempt to illustrate the interaction of some genetic and environmental factors in IHD.

On figure 22, I have tried to assign various elements in the "risk factor" family to a place in the concept of mechanisms, in order to get some kind of understanding of what is "medical" and what is "psycho-social". It may well have to be changed in many ways.

Still it might contribute to make the split less wide between those who like WHO and Laurence Hinkle (68) do believe more in the

"medical" hardware than in the "psycho-social" software, and, on the other hand, the zealous psycho-somaticists.

Despite his upbringing close to Harold G. Wolff and being the director of a laboratory of Human Ecology, Hinkle found "standard physical and metabolic risk factors" to identify men who subsequently developed coronary heart disease to a far greater extent than results from psychological test patterns. Hinkle, who has watched his Bell System employees for a long time, however, also states that "the patho-physiological process which determines the subsequent risk of coronary heart disease among men in this population had already been established by the time they reached their 20's, and this was little influenced by what happened to them thereafter". Therefore, future investigations "should be more centered upon the period of childhood and adolescence than they have been up to this time". This is precisely what is suggested in another WHO-document, by de Haas, last year (69). And it is in conformity with conclusions in an important, but largely forgotten, study by Hardin Jones in 1956 (70), in which he claimed that factors eventually determining life expectancy in different populations were chiefly to be traced back into childhood and youth rather than to later years. So, there we are - caught in the contemporary maze of psychology: whether to attach more importance to early formative years or to the pathogenic situation of the present in our attempts to explain the why? and when? of a heart attack.

Prevention: its feasibility, aims and consequences

This, finally, leads us down to the question of prevention, its real feasibility, its possible aims and its, perhaps inevitable, consequences.

In the beginning of this lecture, I recalled the pressure we felt as clinicians, as the number of myocardial infarcts admitted to our wards was climbing every year, at times almost every month. The urge to act was strong: The coronary care unit to many of us became an immediate answer. But those of us who had been engaged also in epidemiological research knew that this was not a final answer and not a complete answer. We were looking around for ways

and means to prevention, the first link in the chain being identification of susceptibles, the second methods of interference with pathogenic mechanisms.

To-day I believe that most coronary care units have reached a steady state. The infarct rate is levelling off and further technical improvements may well turn out to be close to the point of diminishing returns. Instead, the CCU techniques are being used for improving the care of patients with other dysrhythmias, pulmonary embolism and severe cardiac failure. It would be natural to have a second look at prevention, particularly so-called "primary" prevention of healthy, but "susceptible" persons.

Whenever the word prevention is used in connection with ischaemic heart disease, I take it to mean "post-ponement" of serious clinical manifestations. For most people, the aims are thought of as post-ponement from "active" age to later years. Not everybody realizes that it may also mean: from later years to very old age. The consequences may, therefore, in part be a considerable increase in the old population. With this, other social and medical problems receive increased emphasis, viz., the care of the aged.

Up to the present time old age, in a great number of instances, has carried with it an accumulation of ailments, disorders and diseases which - together with isolation in the four- or even five-generation society, reduced financial resources, faulty memory, lack of purpose and other limitations - has led to an ever increasing demand for dreaded but inescapable institutions for custodial care.

Many younger people have already observed the writings on the wall. In an enquiry to a fair number of Swedes over the last few years by one of our weekly magazines (Table XI), one of the questions was: How do you want to die? A big majority, particularly among the men, indicated that they hoped to pass away rapidly and without warning (71 a,b).

What cardiologists all over the world rally to prevent appears to be precisely what many "at risk" seem to prefer. And not only men: A few days ago, a very clever and sensible lady asked me, if I could advise her about a reasonably safe and certain way to

HOW DO YOU WANT TO DIE ?

	Men	Women	Total
Number	131	64	195
Rapidly	49	14 (+1)	63 (+1)
Without noticing	7	4 (+1)	11 (+1)
During sleep	11 (+2)	7	18 (+2)
Quietly	12	10	22
Prepared	22 (+1)	11	33 (+1)
Living	11	7 (+2)	18 (+2)
Sailing	1 (+1)	1 (+1)	2 (+2)
Without pain	4 (+5)	1 (+4)	5 (+9)
Alone	1	1	2
Never	4	2	6
Evading the question	9	6	15

Answers within brackets: a second attribute given in the answer.

Table IX

Tabulation of answers to the question: How do you want to die? in the Swedish magazine Vecko-Journalen.

be assured of dying a cardiac death (in preference to other ways out).

As to the feasibility of primary prevention, I have tried to list some prerequisites (Table X):

Prerequisites for Primary Prevention (1974)

- x 1. The mechanisms of the disease must be known and methods to interfere with them be available.
- x 2. Simple methods to identify "susceptibles" ("risk factors", "indices") must be available.
- 3. The identification should have a reasonable degree of selectivity and specificity. (?)
- 4. There should be a reasonable time-relationship between recommended action and palpable results.
- x 5. "Susceptibles" must be willing and able to co-operate by changing their mode of life (or taking "prophylactic" drugs),

or

- 6. Authorities (governments) must be willing and able to impose such changes upon "susceptibles" or the population-at-large.

(x denotes items proposed in 1962)

Table X

Up to the present time, such prevention has to be performed by manipulation of the environment. "Environment" is the part of the "mechanisms" that might be manipulated. As yet, and for some time still, fortunately, human genetics cannot be manipulated.

When, twelve years ago, I was discussing the same topic (72), the figure contained items 1, 2 and 5. This time, I have added items 3, 4 and 6. The reason for this is as follows:

It has become increasingly clear, that several of the conventional "risk factors" are not too specific (62). Many seem to be indicators of a generally poor prognosis, a "premature aging" as it were (73), leading to death from a variety of causes, including cancer. (While lack of specificity may make prevention less interesting to the cardiologist, this may not apply to the patient.)

Furthermore, the correlations between "risk factors", findings at coronary angiography and time and mode of death, are not very

strong, and many patients with high risk scores remain healthy over long periods of time, while some low risk individuals unexpectedly succumb to the disease (74). It may well be that death from ischaemic heart disease follows 3 different paths:

1. those with a defined (limited) disorder affecting metabolic processes and/or pathological anatomy and, therefore with shortened life span;
2. those with "generalized" premature aging, and
3. those developing the disease as a component of normal aging.

With regard to prevention, we do not know how much of "premature aging" - or late aging for that part - is genetically determined and how much it depends on factors in the environment - including what has been labelled "social heritage", inherited habits. To interfere with genetics, at this level, seems difficult and dubious. As regards the truly environmental factors, the greatest impact may derive from general developments within the society rather than from selected items thereof. Or perhaps: profound selective changes may not be feasible other than within the framework of general changes. For example, there is clear evidence that the mortality from ischaemic heart disease ("atherosclerotic heart disease") and diabetes was reduced in Sweden during World War II: we have never had a better state of health than some of those years.

It may be that data on cigarettes, cars, saturated fats and other easily measurable commodities could serve as indices of changes in a society. So far, keeping an eye on these figures has not been helpful in predicting changes in the mortality and mortality pattern of ischaemic heart disease in Sweden.

If Flodérus' concept, that some of our vices represent the individual's attempt to balance his "instability", is anything near right, one can wonder what will happen if cigarettes and liquor became suppressed: even in the presence of Sir Richard Doll, and as a non-smoker myself, I venture the suggestion that such soothers are used at least in some instances by people who need them.

Around 1970, my colleagues in Gothenburg, who have been making a magnificent effort to study a large population sample by epidemiological methods, were very enthusiastic about primary prevention (75, 76), while I expressed some reserve, because of the tremendous demand on resources such an endeavour would represent (77). Tibblin, thus, has calculated that in order to "save" six persons, two hundred would have to receive, and accept, "prevention" (78).

A few years later, however, even ardent preachers of the primary prevention gospel, faced with not only the enormous volume of cases to be taken care of, but perhaps even more, with the increasing understanding of the impact of heredity, the non-specificity of many "risk factors" and the possible importance of "the pathogenic situation" (Selye) rather than the pathogenic agent as such, have become converts to the creed of secondary prevention (78) instead.

However, Rahe and co-workers (79) have remarked that if the build-up of precipitating factors were also taken into account - I presume continuously over the years - a better warning of the approaching acute event might be obtained. Whether one will ever be able to evade the closing-in of such precipitating factors as make "the native hue of resolution be sicklied over by the pale cast of thought" I cannot tell, but I doubt.

"Then, what is the question?"

In this lecture, I have tried to discuss, from our experiences, whether ischaemic heart disease is to be regarded as a "medical" or a "psycho-social" disease and the implications of these concepts with regard to prevention. I believe this survey of research performed in only one of perhaps several hundred institutions all over the world has shown that both these aspects have stimulated inquiries into the origin and mechanisms of that disease. Despite an enormous amount of data we have made no great advances with regard to the main body of the problem.

One may remember that curious woman, Gertrude Stein, who on her way into an operation theatre asked her friend, Alice B. Toklas:

"What is the answer?", and as no answer was forthcoming, continued: "Then, what is the question?" - I believe we have had a whole lot of questions (referred to in Table II); some of them have got partial answers over the last fifteen-twenty years, and this has led to revisions of the original questions and shifts of emphasis in our searching. If I should venture to present my personal feeling of this shift it may perhaps look as in Table XI.

Possible shifts in research emphasis


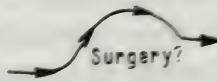
<u>Less</u>	<u>More</u>
The coronary artery	Small vessel disease (?)
Thrombosis, macro-	Thrombosis, micro-
Serum lipids	Lipid (and carbohydrate?) metabolism in a wider setting
The myocardial infarct	The irritable myocardium (and modifying factors)
	Arrhythmias, sudden death
	
Diet	Cigarette smoking
Risk factors, specific	Risk factors, non-specific ("aging"?)
Mass screening epidemiology	Genetics
	Psycho-social factors and their mechanisms
"Invasive" techniques	"Non-invasive" techniques
	

Table XI

This in a way represents a move from the delinquent, the coronary artery, and its pathology, to the target, the vulnerable myocardium and its modifiers, of neurohumoral, metabolic or electrolyte nature, where the deepest secrets still reside (and perhaps the best prospects of therapeutic gains). It may also be taken to represent a move from wholesale, gross, palpable, "specific" pathology to influences of a more sophisticated nature, generated from greater distance, mediated God only knows how: the biological clockwork, setting our allotted time, and the precarious balancing of our instability in response to those "factors that operate through the mind". The difficult problem, the Gertrude Stein question, is not why some people get an infarct or die suddenly, but why some other people, their equals in risk factors and three-vessel disease, do not.

AGE-DISTRIBUTIONS OF DEATHS FROM IHD IN A STANDARD POPULATION, 1968-1971

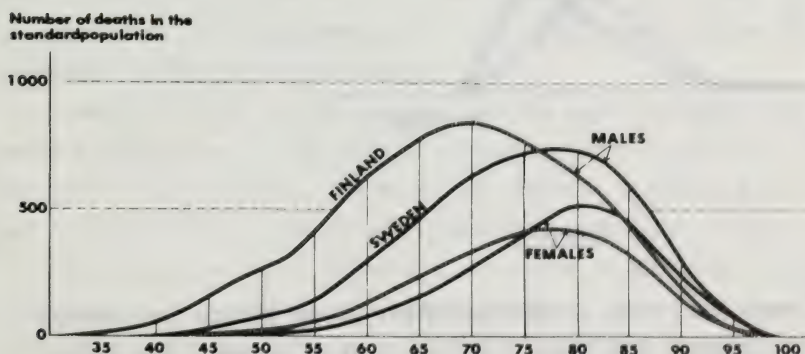


Fig. 23

If you look at the curves for male and female deaths from ischaemic heart disease, for Finland and Sweden (Fig. 23), you

may get the impression that there are "male" distributions and "female" distributions, but also that the Swedish male mortality curve somewhat resembles the "female" Finnish curve.

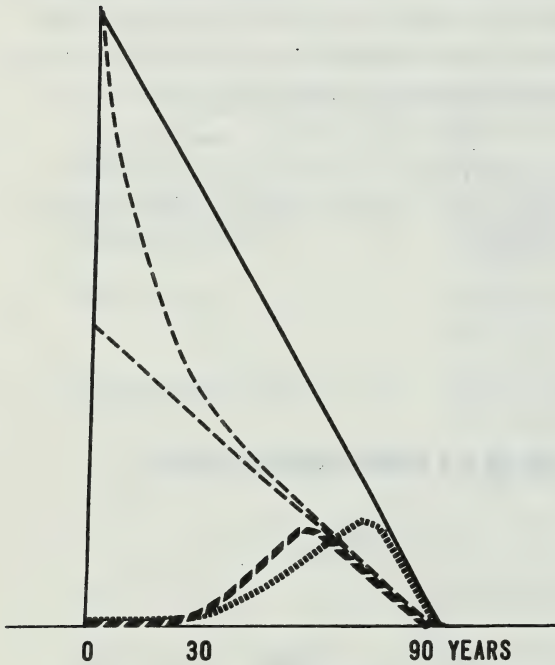


Fig. 24

Two years ago, when I discussed such curves before the Swedish Society of Internal Medicine, I draw a kind of tangent, describing the slope of the latter part of the curve, for nothing better, and I wondered whether this line would have some meaning as an expression of the "life potential" of a group, or of a whole population (Fig. 24). One may then ask: When and how do we lose potential? Do we all start as equals, or is there a difference already from the beginning?

Is there a "biological index" stamped upon us already at birth that follows us along our journey in the space-time continuum we call life, and are endogenous "risk factors" only part of the index?

These are no new questions. Hardin Jones' studies twenty years ago; Paul D. White; life insurance actuaries, Caroline Bedell Thomas and now, a year ago, Lars Werkö (80) in his Gustav Nylin lecture, have all emphasized that the longevity of one's parents greatly determines one's own life expectancy.

In Werkö's material, among 67 men, whose parents both had died before age 66, 15 had died between 50 and 60 years of age, of whom 6 from myocardial infarction, while among 63 men, whose parents both survived to or beyond age 80, only 2 had died during the same period, none of them from myocardial infarction. Twin mortality data from U.S.A. and Sweden recently presented by Liljefors (66), indicate a strong genetic factor in the determination of life expectancy.

In some families, many members attain a high age. In others, there is an accumulation of "premature" deaths. Some of these can be attributed to metabolic disturbances ("inborn errors"), or to an adventurous life - maybe inherited, genetically or through social habits. Why people live into high ages, we know less about. Sometimes, it appears as if "late developers" also live longer. Maybe their clockwork is set at another pace?

However, for me it has been a striking experience over many years to find how, in the hospital wards of some countries, the furrows of the forehead, the windling temporal arteries and the sad and worn-out expression of patients with myocardial infarction contrasted to the more juvenile appearances of patients with the same diagnosis in corresponding age groups in my own country. The same impression has been gained by a competent international medical observer (81). The "wear and tear" of life seems to have left marks with different severity. Or, is this a different rate in consumption of "life potential"? I have personally considerable difficulty in regarding "premature aging" as a "risk factor" as is sometimes maintained. It is just another descriptive term for what we can observe, but it does not tell us more about why and how.

Here at Oxford, where Sir Richard Doll has made an outstanding contribution to the question of "aging" in regard to cancer (82),

it might be tempting to ask for his views on aging and ischaemic heart disease as well.

On the tasks of a Department of Medicine

Some years ago, a distinguished British colleague (83) announced the death of the professor of medicine. I was not so convinced at that time, neither am I now. I hope that my review of what has been going on in our department has shown that I have tried to adhere to Osler's advice regarding the duty of "tabulation and analysis of carefully recorded experience". At least, we are trying to do so. But at the same time we must follow the clues found in the ward or in the laboratory back to where their origin is, or at least as far as we can reasonably arrive. This has always been a clinician's task: his tracks once led to the quarters of poverty and the wells of infection. To-day they will have to carry him also into the world of genetics, or to the computers rattling with data from vital statistics and epidemiology, as well as to the battlefield of behavioural scientists.

No man can embrace all that. Thus far I agree with professor Peart. But unless there can be fostered in young physicians at some - not too distant - point in their career a determination to assume responsibility for a wider perspective, clinical medicine may disintegrate, not through an assault from the outside - which knows that it needs it - but by mere withdrawal from demanding challenges within our own body of peers (84). All too seldom is the voice of clinical medicine heard in our countries in the big and profound issues of our time. I believe no single platform to be more appropriate than that of a department of clinical medicine for participation in the discussion of the future society, a discussion that involves not only "How do you want to die?", but as much, or more: "How do you want to live?".

WHAT TO TELL OUR STATESMEN ABOUT ISCHAEMIC HEART DISEASE ?

A Lilly lecture given on November 20th, 1974,
at the Royal College of Physicians in London

Introduction: causes of disease and effects of "environment"

When the President of the Royal College of Physicians asked me to give this year's Lilly lecture, I tried to ransack my past history to find out what contribution - if any - I might possibly make that could be of interest to this distinguished audience. My background is that of a clinician, starting my early life mainly as a cardiologist, but never abandoning the greater circulation of internal medicine for the lesser ones to the lungs and the heart itself. Perhaps for this reason, I was later offered that post for which professor Peart thinks there is no hope: the professorship in medicine (83).

Unlike my honourable colleague at St. Mary's, however, I believe that such a post and such a person must exist: someone has to be placed where the three circulations meet and be responsible for the propulsion, and the fair distribution, of blood to the various areas, an engineer, caring for the machinery (84).

In such endeavours, over the years, it has become necessary, likewise, to attempt a reconciliation of our concepts of disease, and illness, in the individual patient, on the one hand, and those of the impact of our environment on the etiology and pathogenesis of human disease on the other.

In the times of John Snow (1854) in this very city, the connecting link between the patient with cholera and the environment could be identified as the water-well at Broad Street in Soho. To-day, the causes of major health problems in our part of the world cannot be so distinctly identified. Yet, with regard both to ischaemic heart disease and to hypertension, the search for "causes" - which is a preoccupation haunting physicians and patients alike - has carried many of us away from the circumscribed province of the body and into the vast morass of contemporary society. We are all inclined to project the causes of our personal tragedies on the outside: be it "the evil eye", an unmanageable work-load or capitalism and imperialism-at-large. Only rarely does anybody to-day regard his suffering as punishment for sins committed. But in carrying our case outside our own medical territory, where our competence is rarely challenged, into an

area where most decisions are "political", in the wider sense of the word, we must examine both our arguments and our procedure very carefully.

If we really think that specific factors in our society are "pathogenic" and cause disease we must say so. As medical men we have a three-dimensional image of the human body and its functioning parts. Our environment affects us mainly in as much as it is assimilated and incorporated in us: through our skin, our lungs, our alimentary tract and our sense organs (Fig. 1).

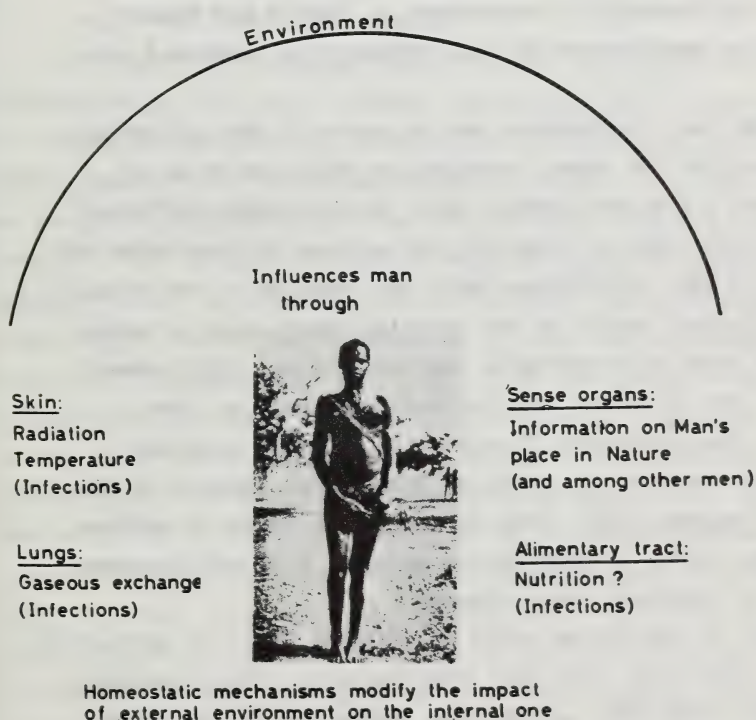


Fig. 1

Some of this incorporation is material, but not all. Man carries an image and a part of his environment within himself and he cannot live without it. Our psychological and philosophical orientation to the outer world - the world we live in - is conceptual and much of what we are dealing with here has a symbolic meaning. Air pollution, dirty water and too much saturated fat in the food may in a very concrete way directly affect the human organism. The way we are affected by the slings and arrows of outrageous fortune is of a different kind, even though one may attempt to measure it by counting "life change events". But much as "mind" cannot be satisfactorily defined in terms collected from, and applicable to, the energetic system - as Sherrington so beautifully and forcefully maintained in "Man on His Nature" - neither can the environment we call "society" be condensed into such terms.

As medical men, furthermore, we are aware of the biological equilibrium within the human organism, as described to us by Claude Bernard and Walter Cannon, with its tremendous buffering capacity in youth and its fragility and aptness to break-down and failure in old age. Interference with one reaction in the complicated physiological mosaic of our organism immediately provokes an extensive chain of homeostatic counter-actions. "Environment" or "Society" are in no way less three-dimensional, or less homeostatic, than ourselves. In advocating changes in either we must always remember the words of René Dubos: "Science is the knowledge of consequences". This is why I have chosen to address myself to the problem of what advice we might give our statesmen with regard to ischaemic heart disease.

Statesmen, in the proper sense of the word, are - by definition, I would say - no fools. They will most certainly transilluminate our arguments before they act on them. Maybe this is the reason why so little action has been taken.

Ischaemic heart disease - historical evolution

Ischaemic heart disease has probably always been with us, even though Heberden was the first to collect and analyze a hundred cases of that disorder which he labelled pectoris dolor, in 1768, before this College. My own hospital - the Seraphimer - dates back to 1752. I doubt that any patients with ischaemic heart disease were admitted at that time. Even in 1909, a year for which I once searched all the records, no more than one patient out of nearly two thousand may have had an infarct (5). In 1959, of the same number of admissions, eighty were diagnosed as myocardial infarction, and to-day, with twice as many admissions, the number of infarcts has risen to more than two hundred.

With regard to ischaemic heart disease, I have personally experienced a time, when the main concern was making a diagnosis of angina pectoris and the subsequent prescription of vasodilating drugs together with common-sense medical advice. From this evolved an interest in diagnosing "latent"(now better: "subclinical") coronary - or ischaemic - heart disease by means of anoxaemia and exercise tests, still on an individual basis and without much repercussion outside the clinical world. But the big epidemiological experiment represented by World War II in some parts of the world did not fail to excite the curiosity of medical scientists, and in the early 1950's I found myself engaged in the international epidemiological campaign conducted by Ancel Keys and my American teacher in cardiology, Paul Dudley White. I cannot mention his name without recalling the unique blend of experience and wisdom with persistent curiosity and youthfulness of the mind, which made him an unequalled medical ambassador of good-will and the first and foremost in our profession to give medical advice to statesmen throughout the world.

These international epidemiological studies, in combination with the prospective investigations in Framingham, Massachusetts - as well as professor Morris' classical examination of bus-drivers and bus-conductors in this city - established the concept of "risk factors" of various kinds, and the hunt for such factors - and for persons harbouring them - has been going on ever since.

Parallel to this extrovert activity, the bringing together of previously scattered knowledge and experience with intensive care units created a situation whereby the mortality in patients brought to hospital with acute myocardial infarction, after decades of insignificant improvement, was drastically cut to half of what it used to be.

What would a statesman want to know?

These have been the two main areas in which research and developments concerning ischaemic heart disease have taken place during the last decade. It has been the privilege of my collaborators and myself to be so placed that we have been able to work in both areas simultaneously and I will try to incorporate some of our experiences in my presentation to-day.

Both these areas, however, are making big and increasing demands on our society, on the allocation of public funds and, in some respects, also requires the establishment of health policies that may have to interfere with the individual's freedom in choosing his way of life. Medical men, who constantly watch tragedies and who sometimes think these could have been prevented, if proper action had been taken in time, are apt to make generalizations and suggest, or even propose, over-all actions to correct faults or inadequacies in society. In this endeavour they may not always take into account the total effects of interference with the biological or social homeostasis. Before we proceed much further, it may be pertinent to consider how those who are the target of our good advice, or our propaganda, might try to assess the evidence presented to them. I have tried to sort out some of the possible questions they might pose, not only with regard to ischaemic heart disease, but to any chronic ailment, for or against which political action is requested.

What would a statesman want to know?1. What is the size of the problem?

Who and how many are affected with regard to sex, age
and occupation?

2. What are the average duration of illness and disability and the demands on hospital and other institutional care?3. What is known of the causes of disease?

What do the experts agree upon, and what not?

4. What would be the aims - and consequences - of actions to prevent the disease?

Are the motives economic or humanitarian?

5. What can the medical profession itself accomplish?6. What would be the tasks of political action?7. What does this all mean to myself?

What do I want with my life?

What could I make use of personally?

Table IThe size of the problem

Trying to find the answers to such questions before a British audience I must, however, apply double book-keeping, because precisely in the quantitative aspects of ischaemic heart disease (IHD), your country and mine show considerable differences, and these differences will affect the "political" estimates of the severity of the problem. The data I am going to discuss derive from the international statistics of WHO and have been worked out in collaboration with the Swedish Central Bureau of Statistics (85). Let me also state, that we have very little reliable over-all information on morbidity - incidence, prevalence and duration of illness. Concepts of morbidity must to a certain extent derive from

data on mortality in combination with experience concerning the natural history of the disease and its prognosis.

When the impact of ischaemic heart disease as a major cause of death became apparent after World War II, attention was focussed upon the considerable differences in mortality rates from such diseases reported from various countries. Great efforts were made to investigate whether the differences were real or mainly due to different medical concepts and traditions regarding death certification. Over the years, international exchange of information appears to have established that some differences are real, so that comparisons between at least some countries during some periods are justified. We have, thus, assembled vital statistics data from England & Wales and Sweden and also from Finland, because this country, our neighbour, is known to be top-ranking in the world with regard to ischaemic heart disease-mortality, together with U.S.A. In this comparison of a high-rate country, Finland, and a low-rate country, Sweden, England places herself in the middle. This means that any change in the British panorama of diseases, and particularly in the prevalence of ischaemic heart disease, might be projected against data from the two other countries. We have attempted to direct our analysis in part to the details of the relationships mentioned and in part to the trends as they have manifested themselves over the last twenty years. At the same time, the differences observed invite questions of "why" and "how", and may serve to illustrate the effects of changes, spontaneous or "manipulated", in the panorama of diseases and their impact on the life-expectancy and age structure of our populations.

Death rates

As is shown in Fig. 2 A, death rates by age and sex from all causes in the three populations of England and Wales, Finland and Sweden are similar in shape but not in level. The curves for England & Wales are even lower than the Swedish curves in younger age groups, but after age 40 for men and possibly somewhat earlier for women, they move towards the higher Finnish curves.

MALE AND FEMALE DEATH RATES PER 100 000 BY AGE AND SEX FOR ENGLAND & WALES,
FINLAND AND SWEDEN, 1960-1971

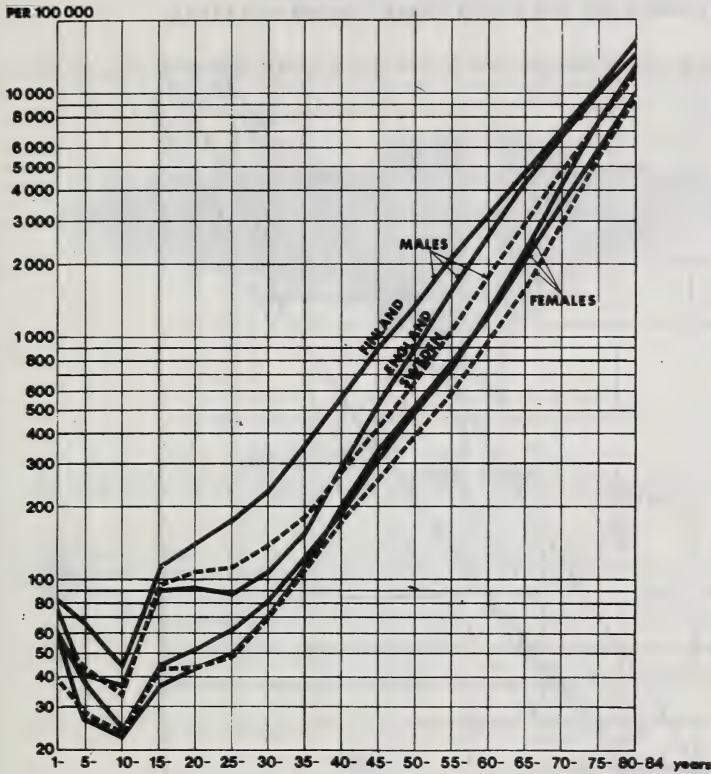


Fig. 2 A

In plain figures (Fig. 2 B), this means that the English male death rate from all causes at age 45 is reached by Finnish men at age 38 and by Swedish men at age 47, while the corresponding age for English women is 49 years, for Finnish women 50 years and for Swedish women 53 years of age.

At age 65, however, the English males have the same death rate as Finnish males of 63 and Swedish of 69 years of age. This rate is reached by English women at age 72, by Finnish at 70 and by the Swedish women at 73.

DEATH CURVES BY AGE AND SEX FOR ENGLAND & WALES, FINLAND AND SWEDEN, 1969-1971, WHERE THE DEATH RATE LEVEL OF ENGLISH MALES AT THE AGE OF 45 YEARS AND OF 65 YEARS, RESPECTIVELY, ARE DRAWN TO SHOW AT WHICH AGE THE OTHER CURVES OBTAIN THIS LEVEL.
Per 100 000

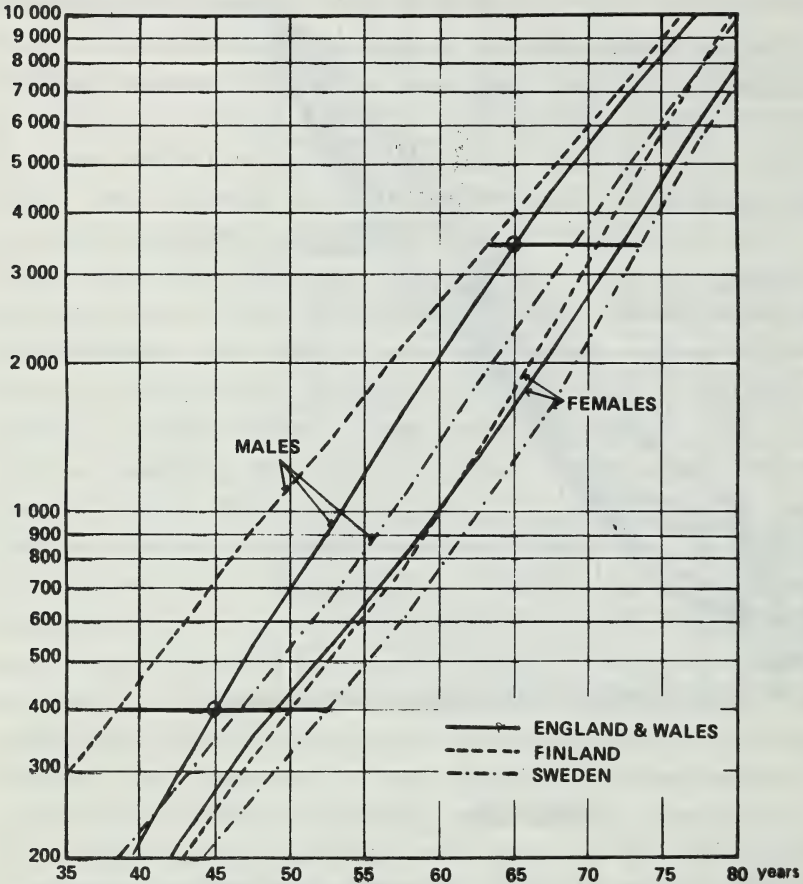


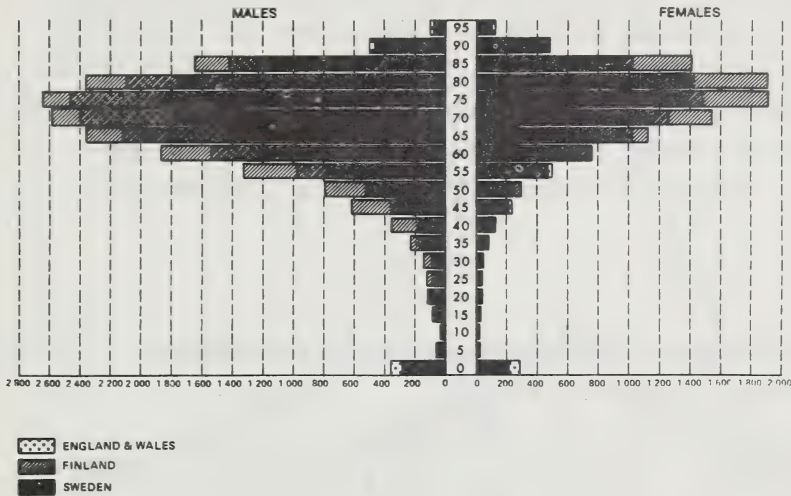
Fig. 2 B

Below age 40, Swedes fare less well than the English. This is due to our higher mortality from accidents and violence, and especially from suicides, and these findings apply to both men and women.

A complicating factor in the comparison of separate causes of death in higher age groups is the fact that far more deaths are ascribed to (chronic) respiratory diseases in England and Wales than in Sweden, Finland occupies an intermediate position in this respect.

Death profiles.

DISTRIBUTION OF EXPECTED MALE AND FEMALE DEATHS IN A STANDARD POPULATION

Fig. 3

A comparison of so-called "death profiles" (Fig. 3) in England & Wales, Finland and Sweden, calculated by applying the age- and sex-specific death rates of each country to a common standard population (=the agedistribution of the total population of England and Wales, 1970) emphasizes the considerable differences that exist as expressions of biological and/or "social" differences between these countries. They have nothing to do with the present - or past - age structure ("population pyramids"), which, as a matter of fact, is remarkably similar for England & Wales and Sweden, but quite different, particularly in the weak upper age groups, for Finland.

When such standardized distributions of deaths from all causes, as well as from cardiovascular diseases and from ischaemic heart disease in particular, for the countries, are presented in

the form of curves with cumulative percentages of deaths along the curves (Figs. 4 A and B), it is apparent, how much later in life the ischaemic heart deaths assume quantitative importance in Sweden than in the two other countries. 50 per cent of the male ischaemic heart disease-deaths have occurred in Finland at age 68, in England at about age 71,5 but in Sweden at age 75, (the comparisons being standardized for differences in age distribution of the countries and also with respect to male and female differences, with England and Wales, 1970, as standard). Corresponding ages for females are around 76 years in England and Finland and 79 in Sweden.

AGE-DISTRIBUTIONS OF DEATHS FROM ALL CAUSES AND FROM IHD IN A STANDARD POPULATION, 1969-1971

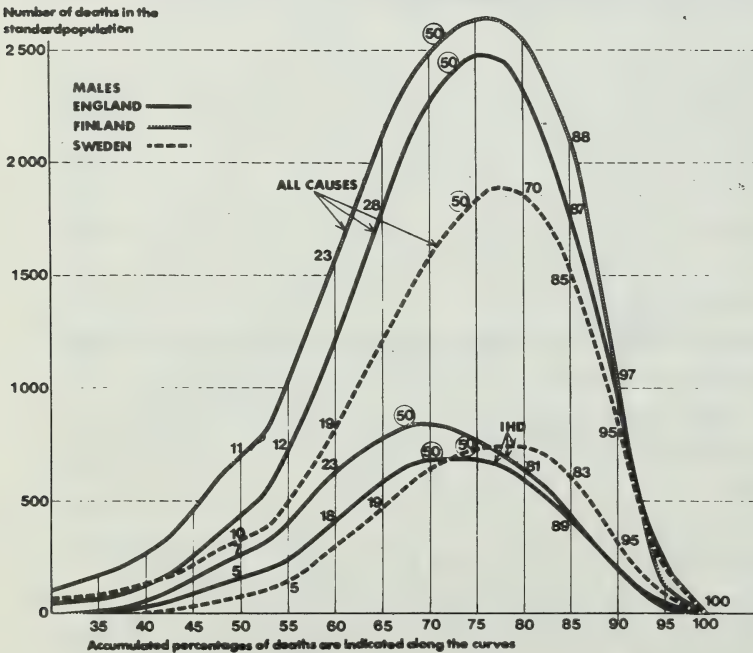


Fig. 4 A

AGE-DISTRIBUTIONS OF DEATHS FROM ALL CAUSES AND FROM IHD IN A STANDARD POPULATION, 1968-1971

Number of deaths in the
standard population

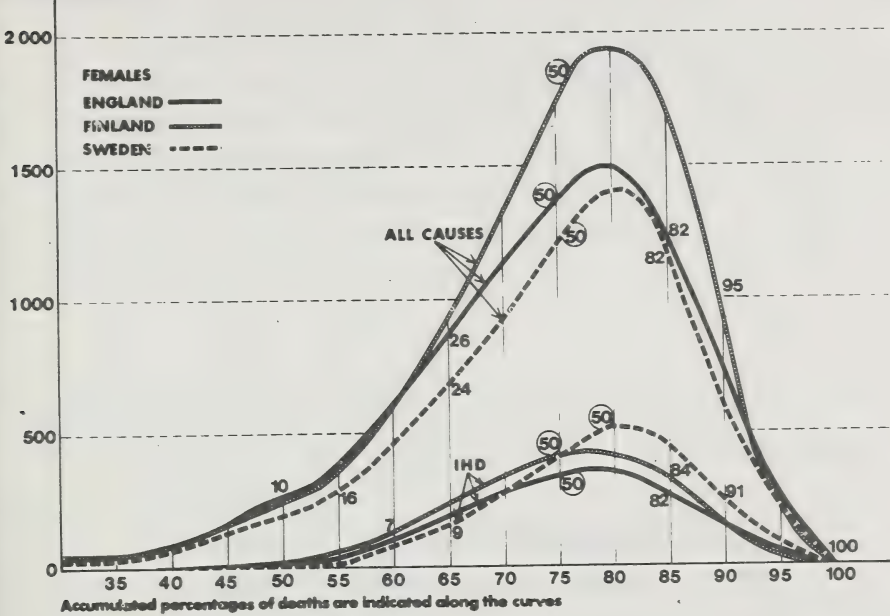
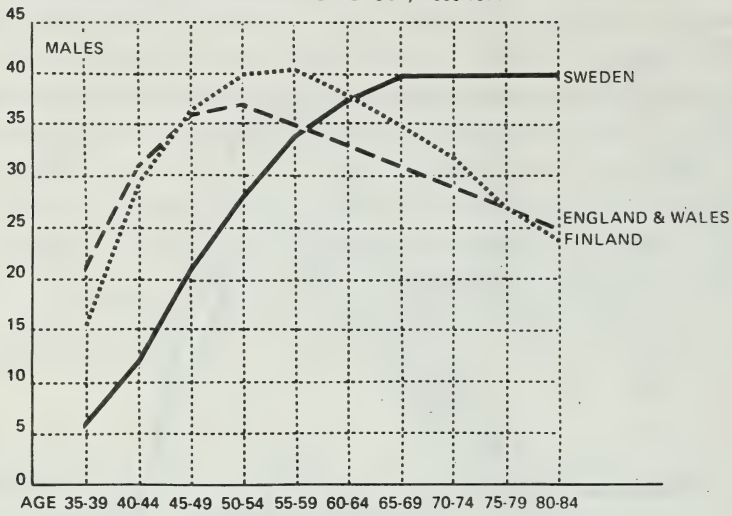


Fig. 4 B

IHD-deaths and deaths from all causes.

Another expression for the tendencies described above is the percentage of deaths from ischaemic heart disease in relation to deaths from all causes (Figs. 5 A and B). This percentage is lower for Swedish men in relation to English and Finnish men up to around age 60, after which age the Swedish curves rise above the English and Finnish ones, which actually turn downwards (in contrast to tendencies in the late 1950's), and place themselves on a plateau around (males) 'or slightly below (females) 40 per cent.

DEATHS FROM IHD AS A PERCENTAGE OF DEATHS
% FROM ALL CAUSES IN EACH AGE GROUP, 1969-1971



DEATHS FROM IHD AS A PERCENTAGE OF DEATHS
% FROM ALL CAUSES IN EACH AGE GROUP, 1969-1971

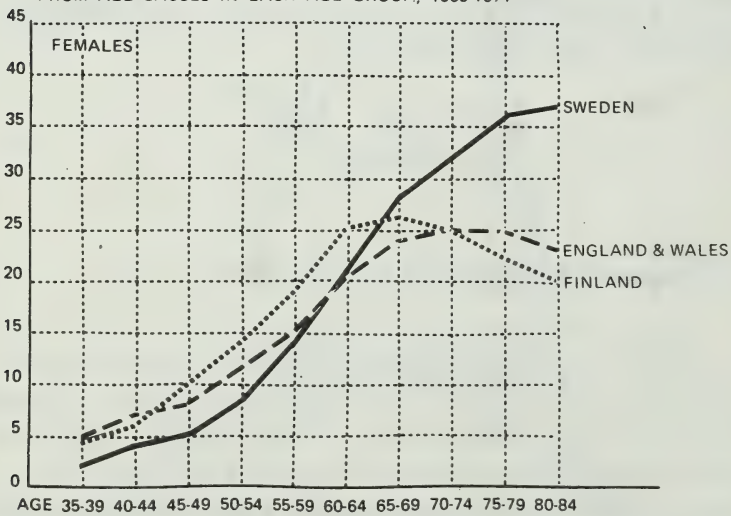


Fig. 5 A and B

In both England & Wales and Sweden mortality from all causes has been diminishing in all age groups for both men and women during the last two decades (1951-1970) (see figures 2 and 3, page 9 and 10). This reduction in mortality has been more apparent for English men - who started from a higher level - than for Swedish men, while the reverse is true for English women in relation to the Swedish ones. Yet, the decrease for English women is faster than for English men. Of particular interest is that only a very small change has occurred over these 20 years in the mortality rates for both Swedish and English men aged 65 - 74 (Table II).

Average annual decrease in mortality, 1951 - 1971, as percentages of mean death rates.

Age	Males		Females	
	England & Wales	Sweden	England & Wales	Sweden
35-39	1.51	0.12	2.07	1.59
40-44	0.53	0.05	0.98	1.39
45-49	0.50	0.21	0.70	2.36
50-54	0.84	0.99	0.72	1.86
55-59	0.69	0.50	0.90	2.04
60-64	0.37	0.19	0.95	2.04
65-69	0.07	0.01	0.99	2.12
70-74	0.04	0.05	1.15	1.89
75-79	0.34	0.14	1.22	1.50
80-84	0.65	0.45	1.22	1.39

Table II

The overall mortality reduction is also seen in the groups of cerebro-vascular diseases and hypertension for both males and females in both countries.

As for ischaemic heart disease (see figures 4 and 5, page 11 and 12) however, both English and Swedish male rates show an upward trend, except for the oldest age groups in England (beyond age 75). This may depend upon your choice of respiratory disease as cause of death here. For all age groups below 75, the English curves are considerably higher than the Swedish ones. In England, for women below 55, there is a tendency of increase in the ischaemic heart disease-mortality, which has no counterpart in Sweden, where the rates are falling in all age groups except above 80.

Possible effects of "prevention".

Calculations made by WHO as to a gain in life expectancy in case of a - very hypothetical - complete elimination of deaths from cardiovascular diseases (86) may look optimistic (Table III), but

Possible gain in life expectancy if deaths from
cardiovascular diseases were eliminated (WHO)

	<u>England & Wales</u>	<u>Finland</u>	<u>Sweden</u>
Males:	68.7 → 76.1 \searrow 7.4	65.9 → 74.5 \searrow 8.6	71.8 → 80.3 \searrow 8.5
Females:	74.9 → 83.9 \searrow 9.0	73.6 → 83.4 \searrow 9.8	76.5 → 86.1 \searrow 9.6

Table III

have to be viewed against the fact that such diseases make up more than 50 per cent of all mortality. However, the "average" age at death from all cardiovascular diseases is in England & Wales for males 70 years and for females 78 years, the corresponding ages being for Finland 67 and 75 years and for Sweden 74 and 78 years. The main effect of such an - unrealistic - proposal would be a considerable increase in the number of old and very old people. To study how mortality influences the population structure and the proportion of elderly, "life table" populations from the three countries have been constructed and the pyramids subsequently super-imposed upon each other (Fig. 6).

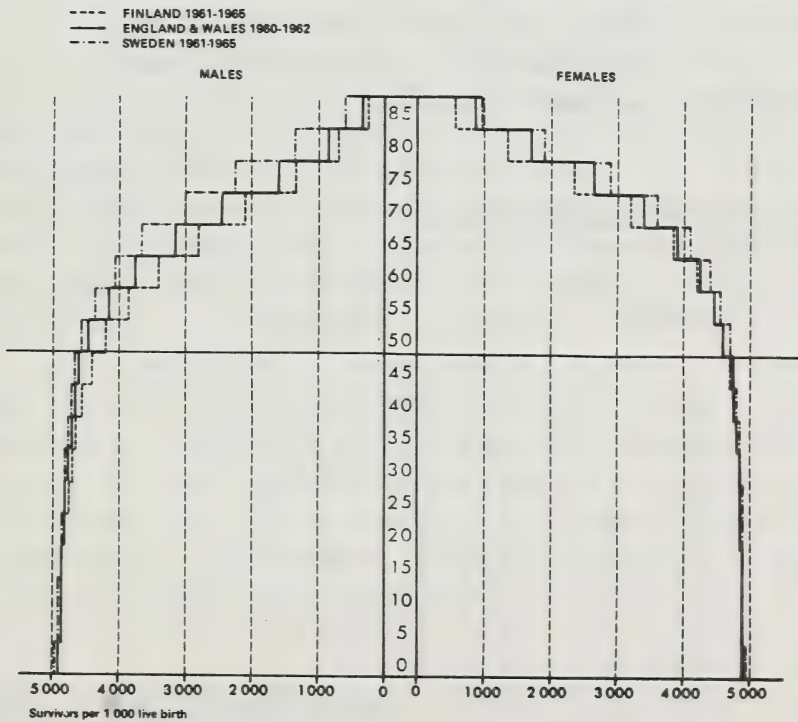


Fig. 6

"Life-table" populations of England & Wales, Finland and Sweden.

Deaths reduce the male population over 50 years of age considerably. The Finnish population, thus, is reduced with more than 40 per cent already at the age of 65 years. Elimination of cardiovascular diseases - which are responsible for more than 50 per cent of all mortality - would in England, or Sweden, have its main impact on people in retirement. Of 60.000 Swedes aged 50, 70 (or fewer) of the men and 12 (or fewer) of the women die from myocardial infarction that very year.

Sudden death

Finally, a note on sudden death. The differences encountered in total ischaemic heart disease-death rates also include a vast majority of sudden death cases. Also in this respect, the figures differ considerably between Sweden and the two other countries (if one may use Scottish statistics to illustrate conditions in the United Kingdom!), as shown in Table IV.

Male "sudden deaths" per 1000 inhabitants
(acc. Romo 1972)

	<u>Stockholm</u>	<u>Helsinki</u>	<u>Edinburgh</u>
30 - 34	-	0.1	
35 - 39	0.1	0.3	
40 - 44	0.3	0.7	} 1.2
45 - 49	0.6	2.1	
50 - 54	0.7	1.7	} 3.2
55 - 59	2.0	4.5	
60 - 64	3.5	6.4	} 5.7
65 - 69	6.0	5.0	
70 - 74	7.7	13.1	
75 - 79	12.8	19.5	

Table IV

The figures presented are not comparable to those presented earlier in this paper, but I have felt it justified to include also this aspect of the subject as it will, undoubtedly, be of importance for the general discussion of what causes the differences between the countries.

Part of the differences observed is probably due to terminology ("sudden death" versus "medically unattended" deaths, whether autopsied or not), in part they depend on time limits set for the concept "sudden": everything seems to "go" between "instantaneous" and 24 hours! (Many cases of sudden death are being ascribed to "acute myocardial infarction" by way of inference, even though no autopsy may have been performed.)

The 1973 "National Heart, Blood Vessel, Lung and Blood Program" of the U.S. National Heart and Lung Institute (87) stated that half of the 400.000 annual coronary deaths are unwitnessed and in half of these, sudden cardiac death is the first evidence of heart disease. Kuller *et al.* (88) reported that 2/3 of all deaths from atherosclerotic heart disease in the Baltimore area were sudden, and only 1/4 occurred in a hospital. More than 50 per cent had a prior history of heart disease. Armstrong *et al.* (89) considered that 1/3 of the deaths from ischaemic heart disease in Edinburgh were sudden, but if 4-week mortality was counted, the figure was 60 per cent.

In Sweden, Wikland (13) found that of all deaths from ischaemic heart disease in the Greater Stockholm area 39 per cent of the male and 22 per cent of the female deaths were "medically unattended", while 37 per cent occurred in hospital and the rest in other institutions. Romo (14) in Helsinki found a 4-week mortality from sudden death in 48 per cent of the men and 33 per cent of the women dying from ischaemic heart disease.

What do these differences mean?

This study has been prompted by the obvious differences in mortality from ischaemic heart disease demonstrated in international vital statistics. In as much as ischaemic heart disease is one of

the greatest single causes of disease and death in industrial societies, and the demand for preventive measures has been strong, it is tempting to speculate on the causes for such discrepancies as have been analyzed in this study in populations whose general social, cultural, and economic level is fairly similar, and where vital statistics data are known to be highly reliable.

To repeat Gertrude Stein's question: "If this is the answer, then, what is the question?"

Of course, there are differences between these populations. The greater part of the Finnish population has a racial origin (and blood group distribution) different from the Swedes and the Anglo-Saxons. England and Finland have both suffered from participation in two wars, while Sweden has lived in peace (though not without nutritional hardships along with the other two nations during the war periods). For those who believe that early life experiences may reduce the life expectancy of individuals, this may be an explanation. Present "psycho-social" conditions may, of course, also be different. Cigarette smoking appears to be one item, in which both England and Finland carry a heavier load than Sweden, so far. WHO collaborative studies (90), however meagre, appear to indicate a lower concentration of trace elements (apart from sodium, which is, however, more than a trace element) in Swedish hearts than in those from other parts of the world.

All of these avenues - and others as well - seem worthy of investigation, for if England and Finland want to tread the road towards WHO's goal of eradicating cardiovascular diseases in general, and ischaemic heart disease in particular, as causes of illness, invalidity and death, then, finding out the secrets of the Swedish ischaemic heart disease-situation might represent at least a step in the desired direction. Why we have arrived where we are, we do not know ourselves.

Duration of illness and demands on care

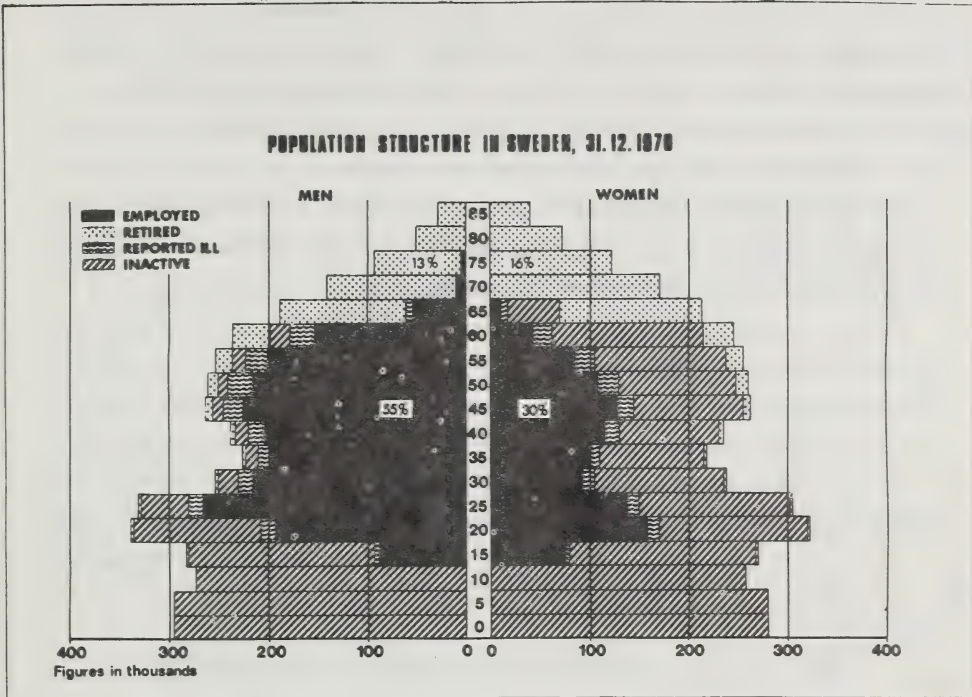


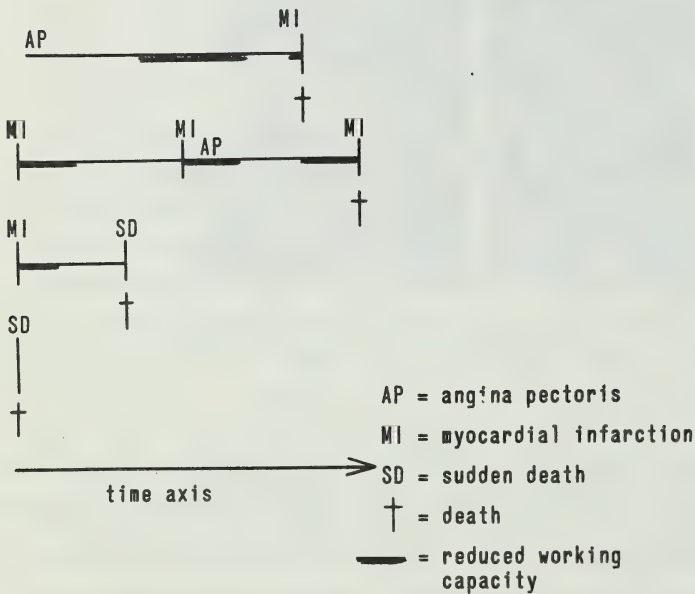
Fig. 7

The Swedish population with regard to the employment situation. There are considerable movements in and out between the various compartments. ("Inactive" = economically inactive).

Politically, morbidity data are probably more important than mortality data. Economically, to speak bluntly, a sick or disabled person before retirement age not only causes an outlay of money for care, but may also detract from society's productive forces - unless he or she can be replaced by somebody otherwise unemployed. In our present societies, the pool of unemployed seems to be on the increase. After retirement, there are the same expenses for care, but no contribution to the national product is expected from the sick person - on the contrary, death puts an end to paying his pension, which is a net gain to the Treasury.

In dealing with the average duration of illness and disability and the demands on hospital and other institutional care I have only had access to Swedish data. It would be reasonable to expect that English data would exceed the Swedish ones with regard to the impact of ischaemic heart disease in so-called productive years, while the demands for prolonged hospital and institutional care in upper age groups would, so far, be less - as yet.

One must clearly distinguish between morbidity in the terms of human suffering (e.g. anginal pain, dyspnea at exertion etc.) and such in terms of reduced working capacity.



Clinical course and socio-economic effects in individual cases.

Fig. 8

The less a society demands crude physical work by its wage-earners, the less these two concepts may relate to each other. Furthermore, reduced working capacity may not be a continuous state, but a temporary one. Death may be the first and only manifestation of ischaemic heart disease, perhaps in as much as a third of the cases.

In Wikland's study (13) of 967 cases of medically unattended deaths in Greater Stockholm, this was the case in about thirty per cent. In the Framingham study (91), sudden death was a first manifestation of ischaemic heart disease in previously healthy people in 14 per cent of the males and 3 per cent of the females. Reduced working capacity due to primary angina pectoris appears to be fairly uncommon, but invalidity from post-infarction angina and latent or manifest cardiac failure, particularly in the years immediately before retirement age, may lead to early retirement. It is a common Swedish experience (92), recently corroborated by Elmfeldt (74) that 70 per cent or more of patients surviving a myocardial infarction and previously employed return to work, mostly to their former job, usually after a period of 3-4 months. Data given to me by the Swedish Pension Board show that of new disability pensions in 1970, 14 per cent of the men and 7 per cent of the women were given their pensions because of ischaemic heart disease (Table V).

Some socio-economic data on IHD in Sweden

Swedish pension age 67 years

A. CCU, Seraphimer hospital 1968-70: 51 % <67 years > 49 %

B. Percentage of all days in Departments of Medicine
(Stockholm and Upsala counties):

Acute myocardial infarction	8 %
Other ischaemic heart disease	8 %
Other diseases of circulation	10 %
	<u>26 %</u>

C. Percentage of patients in hospitals for chronically ill
(Stockholm and Skaraborg counties):

"Heart disease"	10 % (70 % > 80 years)
Cerebrovascular disease	25 % (45 % > 80 years)
	<u>35 %</u>

D. Disability pensions, new cases, 1970:

All cases	Men 19.500	Women 13.200
Ischaemic heart disease	2.700	860
	(14 %)	(7 %)

Table V

However, a look at the "daily allowances" for heart disease (ischaemic heart disease not specified) in the Swedish National Health Insurance system indicates that ischaemic heart disease - as a fraction of "heart disease" - does not represent a particularly heavy economic burden for the Swedish society, at least not below age 67 (pension age).

On the hospitals, however, the impact is much stronger. Acute myocardial infarction is responsible for 8 per cent of the admissions to the departments of medicine and ischaemic heart disease at large for at least fifteen per cent, probably more. As the hospital stay is longer than average in these cases, the patient load at any one time will be greater than appears from the admission rate as such.

As regards institutional care for the chronically ill, cerebrovascular disease counts for very much more than "heart disease", the latter diagnosis apparently being given mostly to quite old people, mainly above eighty years of age. As measured by this yardstick, the prevention of stroke - whether "big" or "little" - seems to be the top-ranking priority within cardiology.

To estimate the prevalence of ischaemic heart disease in any one population is far from easy. Ischaemic heart disease may be thought of as comprising at least four "sets" (Fig. 9).

Four sets of clinical manifestations of ischaemic heart disease

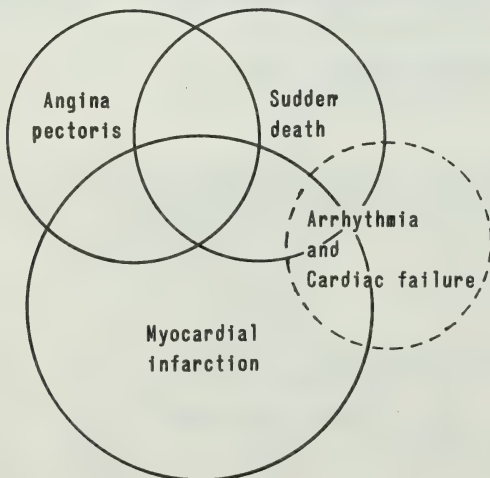


Fig. 9

Of these "sets", some reasonable estimates can be made of AP/MI/SD. "Pure" SD, by definition, makes a limited impact on morbidity.

As regards England, professor Morris (93) has recently stated that "1 man in 5 develops clinical myocardial ischaemia by the time he is 65, and probably 1 in 4 by 70". These estimates appear high to a Swedish clinician.

HEALTH SURVEY: STOCKHOLM, 6,663 PERSONS 66 YEARS OLD (1971)

	<u>Men</u>	<u>Women</u>
<u>Invited</u>	3,898	5,643
<u>Examined</u>	2,724	3,939
<u>Final diagnosis</u>		
412 Chronic IHD	37	18
413 Angina pectoris	30	23
414 Asymptomatic IHD	<u>13</u>	<u>16</u>
	80 (<u>3 per cent</u>)	57 (<u>1,5 per cent</u>)

HEALTH SURVEY: GÖTEBORG, 1,100 PERSONS 70 YEARS OLD (1971)

ECG

<u>Examined</u>	484	571
"Probable IHD"	<u>8 per cent</u>	<u>4 per cent</u>
(Rose, 1965)		

Table VI

Some data from recent health surveys in Sweden.

We have data from two recent comprehensive health surveys, one on 7,000 persons, 66 years old, in Stockholm (94) and one on 1,100 persons, 70 years old in Göteborg (95). There is considerable discrepancy between subjective statements and objective diagnosis. Of the 66 years old in Stockholm, ischaemic heart disease was found in 3 per cent of the men and 1 1/2 per cent of the women,

as a final diagnosis. Electrocardiographic signs of infarction were found in 1 per 1.000. Of those 70 years old in Göteborg, 8 per cent of the men and 4 per cent of the women had "probable evidence of ischaemic heart disease" (acc. to Rose) in their electrocardiograms.

In conclusion, in my country, morbidity from ischaemic heart disease may be more important as a cause of suffering or insecurity than as a cause of reduced working capacity, and the demands on short spells of acute, hospital care are, relatively, more impressive than those on long-term care in institutions. These patients, apparently, either manage to take care of themselves - or die.

Causes of ischaemic heart disease

Against this background of data on the impact of ischaemic heart disease on the populations of our countries I will now turn to those questions which could reasonably be asked by our statemen, namely: this being so, what are the causes and can they be influenced by general, "political" means? If so, what would the end results be?

Let us try to answer the first part of this question: our present state of knowledge regarding causes and the means at hand to dispose of them. We have all heard so much about "risk factors" for the last 10 to 20 years, that we may have become indoctrinated with them. Most large epidemiological or clinical studies have arrived at the same kind of "Top ten" lists, with cholesterol, hypertension, cigarettes etc, as the leading culprits, with other items lower down, such as physical inactivity, diabetes, hypertriglyceridaemia, electrocardiographic abnormalities, overweight, personality pattern and soft tap water. In some materials, one or the other of these items comes out of the computer with one, two or three stars of statistical significance in the separation of

groups; in other studies one or the other of the items does not reach such significance. An interesting and confusing fact is that with the same "risk factor load" in certain groups, morbidity and mortality figures may differ widely between countries, e.g.

Americans have twice as high morbidity as Europeans (96). Why is that so? And why do you and we differ five years or more in some age groups with regard to the male mortality in ischaemic heart disease?

One disease or several?

I believe that the real problem concerning the "risk factors" is conceptual rather than statistical: to what class or level in our overall concept of "ischaemic heart disease" do these factors belong? I have repeatedly over the years been asking the questions: is "ischaemic heart disease" one disease or several? I shall not repeat this question here, because it would carry too far to try to answer it, but, personally, I am convinced that we will soon arrive at a point where we can discern certain combinations within the mosaic made up by different etiologies, different pathophysiologicals and different clinical manifestations. Lars Werkö (80), in his recent Nylin lecture, likewise, expressed his misgivings concerning the popular concept of an indivisible coronary heart disease.

However, even though one might recognize a variety of clinical entities in ischaemic heart disease, this may not necessarily mean different "diseases", and a patient may be moving from one pattern to another, clinically, while suffering basically from the same pathological process (Fig. 10). This is so with many chronic ailments (24).

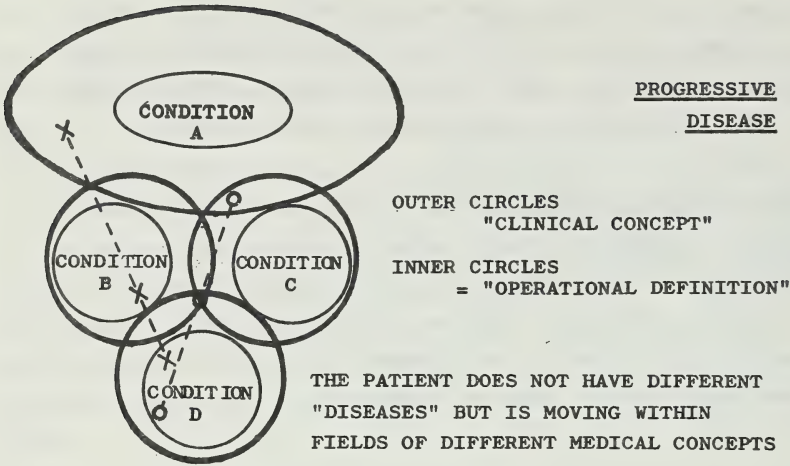


Fig. 10

Contrasting concepts and the meaning of "risk factors"

In order to illustrate the complexities in dealing with ischaemic heart disease, I tried for myself to list a number of "contrasting concepts" (see table III, page 24). Of particular importance in the discussion of community action against ischaemic heart disease is the interpretation of the "risk factor" concept (Table VII).

Are "risk factors" to be regarded as "causes" or merely as "indicators" of something deeper and less well understood? Are some of them spurious and only identified as "risk factors" because of their association with other, known or unknown, factors? From what we seem to know, "soft" water areas have more ischaemic heart disease than "hard" water areas. Is calcium protective against what the Americans call "hardening of the arteries"? Or does this observation only indicate that sunny areas are more healthy than rainy ones? Is cigarette smoking a "cause" of ischaemic heart disease, or is it its association with drinking that creates an over-mortality from many causes, apart from lung cancer, such as

"Risk factors"For a "First myocardial infarction":

Parents' early death	"Type A" personality
High cholesterol	Physical inactivity
High blood pressure	Overweight
High triglycerides	High cigarette consumption
High hematocrit	High alcohol consumption
High E.S.R.	Accumulated "life changes"
High uric acid	
Diabetes	Chest pain. Dyspnea.

Soft tap water area.

For any subsequent infarct:

Age	Non-adherence to treatment
High respiratory rate	- antihypertensive
High transaminase values	antiarrhythmic
High arrhythmic tendency	anticoagulant
	exercise

For sudden death (in particular):

Ventricular ectopic beats	Cardiac enlargement
Bradycardia	Triple vessel disease
Minor QRS conduction defects	Previous myocardial infarction

Physical inactivity. Excessive smoking.

Table VII

ischaemic heart disease, accidents and suicide? Or do we have to probe deeper into the personality traits to find the real mechanisms?

We know that the conventional risk factors are not operating uniformly during the whole course of the disease. Some factors increase the risk for a "first episode" of ischaemic heart disease

of one type, but later on they lose much of their importance and give way to others, which then take over. This is, of course, of relevance for any decisions to be made with regard to preventive measures. Still, the basic question remains, whether removal of "risk factors" of one kind - if at all possible - will reduce morbidity, or postpone mortality, from the particular disease, or even from other kinds of disease. "Causes" relate to "concepts": on what part of a life-long process we are focussing our attention and - if we want to interfere with the process - what the alternative course is likely to look like.

However, the early, short list of "risk factors" has been considerably extended in later years. At the same time, it has become evident that many are nonspecific, and do indicate increased risks for death from other causes as well. "Premature deaths" from ischaemic heart disease may, therefore, in part be conditioned by factors that promote premature aging in general. It may well be that we have to do with at least three groups of victims of ischaemic heart disease:

1. those with a defined (limited) disorder affecting metabolic processes and/or pathologic anatomy and, therefore, with shortened life span;
2. those with "generalized" premature aging, and
3. those with the disease as a component of normal aging.

"Premature aging" is not a "risk factor" in itself. It is the expression of a biologic phenomenon and this is geared to genetics. Ischaemic heart disease is only one of several manifestations thereof.

Extensive twin research, carried out in our department - about which I reported in greater detail at Oxford - has led us to believe that genetic factors truly are powerful movers in the development of ischaemic heart disease. This influence, however, seems to be more clearly expressed in women than in men and the only sensible explanation for this seems to be that "environmental" (exogenous, psycho-social) factors - up to the present time at least - exert a stronger influence on the "male society".

Thus, genetics and "environment" - taken as the stimulation by exogenous factors of responses for which endogenous potentialities already exist - seem to meet here. Expressed in psychological terms, derived from Eysenck, as is done in a recent Swedish thesis (60), the "susceptible" candidate for ischaemic heart disease basically is an unstable person, trying in vain to balance his lack of stability in an unyielding environment by "behavioral coping": smoking, drinking, overwork etc.

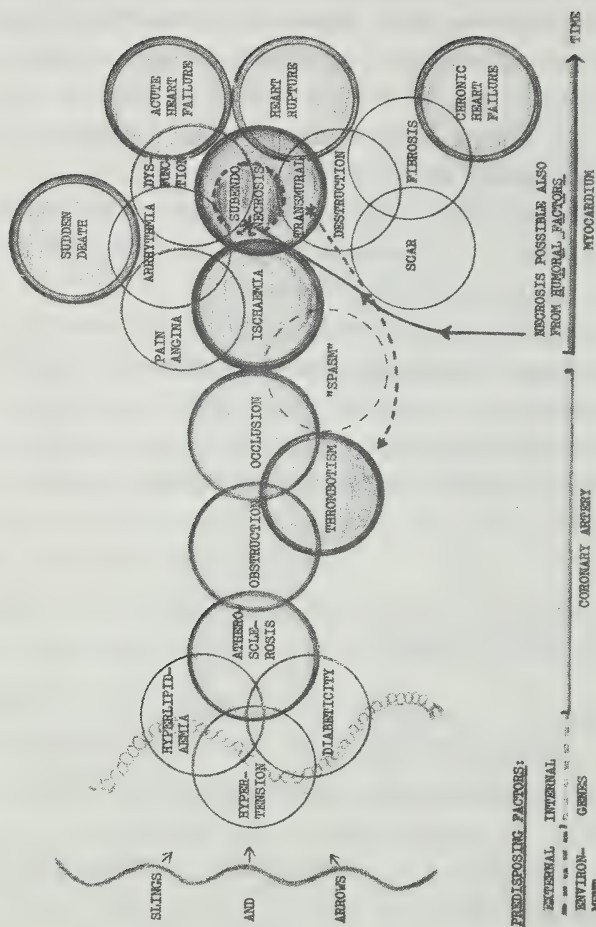
One cannot take man and his environment apart and handle them separately. Free-living human beings may seek the outer environment that is most compatible with their genetic code.

In the last letter I got from Paul D. White, in February, 1973, he wrote on this score: "We are very close together in our thinking and I have been tending in this direction for the last decade or more, chiding some of the epidemiologists for overmuch emphasis on environmental risk factors and not enough emphasis on the genes and the individual."

A pluralistic yet unified concept

To paint a picture of ischaemic heart disease, which everyone would accept, is impossible. Here, as always, so much depends on the angle from which the object is viewed. Yet, I have made a desperate attempt to include the major items in a picture representing the pathogenesis of ischaemic heart disease and its clinical manifestations by way of a series of modified Venn-diagrams (Fig. 11), and in accordance with contemporary vocabulary I have called it "A pluralistic, yet unified concept of IHD".

A PARALYSING, YET UNITED, CONCEPT OF I.H.D.



ALL PARTS OF THIS CHAIN OF EVENTS ARE INDEPENDENT THOUGH USUALLY CONNECTED

Fig. 11

I am certain that one can argue about many things in this picture, but I do hope that somehow it would fit the request of our statesman that most "experts" should agree upon it. Each expert would, however, be free to inflate his pet balloon. Personally, I would like to comment on a few items:

Certain metabolic processes, and their extremes or deviations in particular, especially if they are combined with hypertension, are important predisposing factors for the development of atherosclerosis. Such factors are to a great extent genetically determined, but the extent to which they manifest themselves may depend on the environmental conditions.

The formation of coronary arterial thrombi is conditioned by various humoral factors. Thrombi may develop and progress both before and after myocardial necrosis, thus, being both cause and effect of a myocardial infarction.

Ischaemic heart disease is, by definition, caused by insufficient coronary arterial blood supply, which may be the result of occlusion of large coronary vessels or of other circulatory mechanisms. The former is the probable mechanism in the majority of transmural infarctions, whereas the latter is most often the cause in subendocardial infarctions (23). Similar pathology may also be caused by damage to myocardial cells from other causes, e.g. humoral or metabolic.

Spasm may play a role in Prinzmetal's angina and possibly also as a factor producing stasis in coronary arteries in myocardial infarction, enhancing the formation of coronary thrombi.

Transmural and subendocardial infarctions differ in many aspects, both clinically and pathologically (22). Transmural infarctions are larger, have a higher mortality and more complications, some of which virtually never occur in subendocardial infarction, e.g. rupture of the ventricular wall or septum. The clinical picture is usually more "typical" and the infarction is more easily diagnosed on ECG. In contrast, subendocardial infarction is usually less extensive and has a lower mortality as well as less serious complications. The diagnosis is often impossible to make on ECG, since the changes are non-specific. However, death from arrhythmia is not uncommon.

There are no cigarettes in the picture. They may, nevertheless, exert their undisputable influence in two ways:

- a) as an expression of a genetically determined behaviour pattern associated with an increased incidence of ischaemic heart disease (and several other pathological conditions) and/or
- b) as mediators of humoral changes in the internal environment of myocardial cells (i.e. catecholamines).

Treatment of high blood pressure will reduce the incidence of strokes, renal derangement and chronic cardiac failure, but may increase the mortality from myocardial infarction and possibly arrhythmias (diuretics-electrolytes).

It is not known what the ultimate changes in the causes of death would be, if hyperlipidemia and diabetes ("diabeticity") were alleviated.

There is little in this chain of events that could immediately explain the differences in mortality rate between England & Wales and Sweden. It is, however, clear that obstructive lung disease is much more prevalent in your country than in ours and there are reasons to believe in an association between such conditions and ischaemic heart disease. Cardiac arrhythmias appear to be very frequent in advanced obstructive lung disease. The cause of death to be reported may in fact depend on the circumstances, under which the death occurs.

Predisposing and precipitating factors

The picture just discussed has perhaps given an impression of a smoothly "rolling" chain of events, entering somewhere to the left and passing away through an exit to the right. But somewhere, in-between the two main parts of the chain, there is a precipitating event, that turns the potential danger of the predisposing factors, the accumulated "risk", into the reality of life-threatening disease.

THE ACUTE EVENT

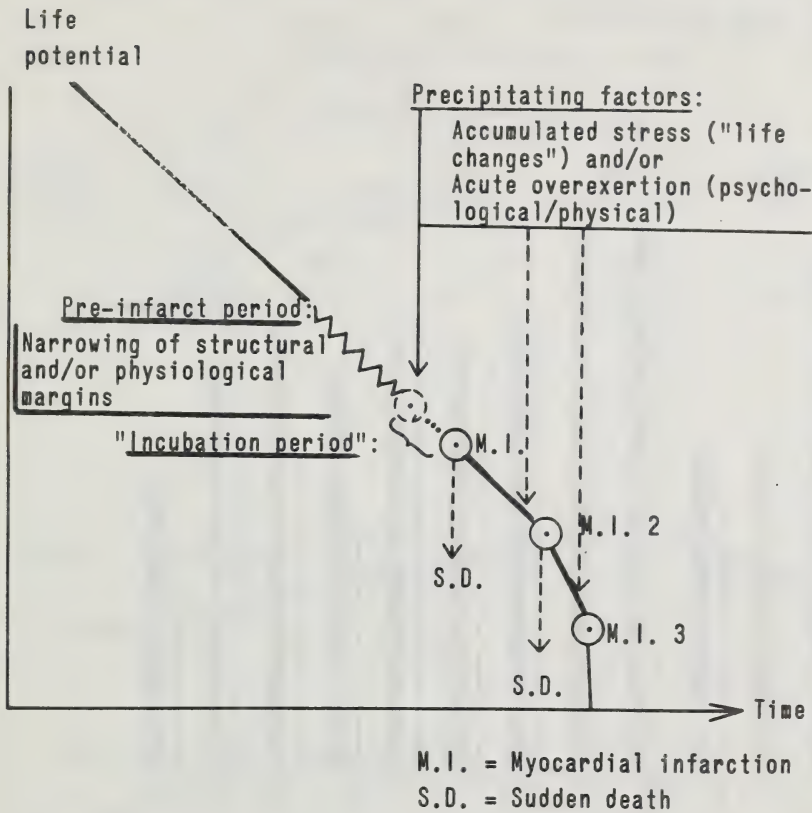


Fig. 12

The predisposing phase is long; the precipitating event may be short and intense like a lightning, but is probably more often represented by the last straw breaking the camel's back - or merely the work of chance. Of this we rarely know anything, because we cannot yet identify the "incubation period" (Fig. 12). It appears as if infarct patients are brought to hospital most often during the active part of the day; if the duration of symptoms is estimated, the beginning of symptoms seems to occur more often in early morning

hours than during midnight (4, 97). Patients who develop symptoms outside their homes seem to arrive in the hospital earlier than those who stay at home (12).

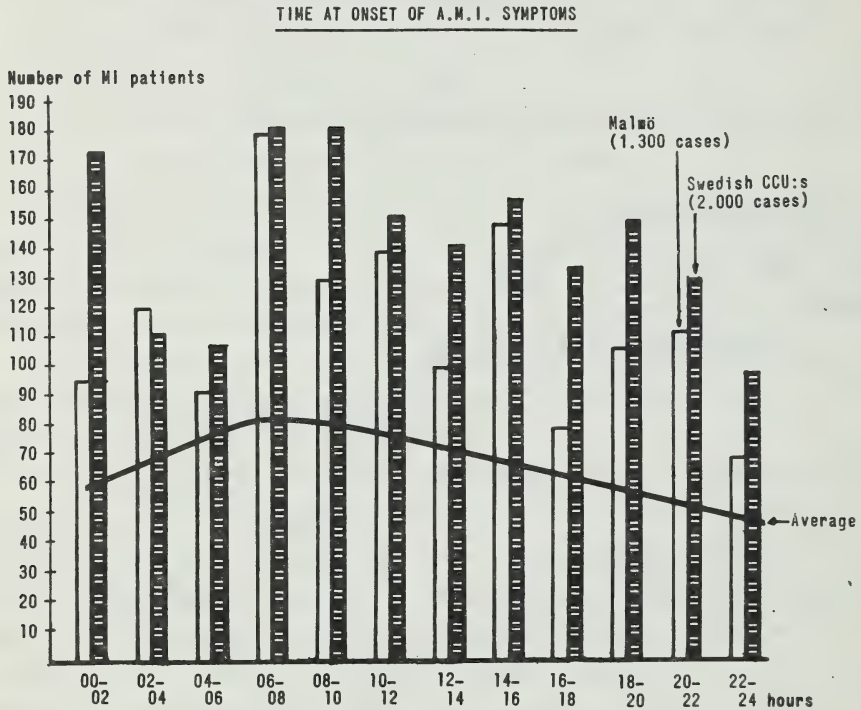


Fig. 13

Diurnal rhythm of acute myocardial infarction.

The precipitating factor releases a chain of events; some of these can be objectively verified if the patient is seen by a doctor, others remain purely subjective and may under certain circumstances escape notice or be misinterpreted ("silent infarcts"). In our experience, symptoms in the form of pain most often precede the general ones. However, in elderly patients, symptoms are often less distinct. Syncope and pulmonary oedema, though, may well precede pain (Fig. 14).

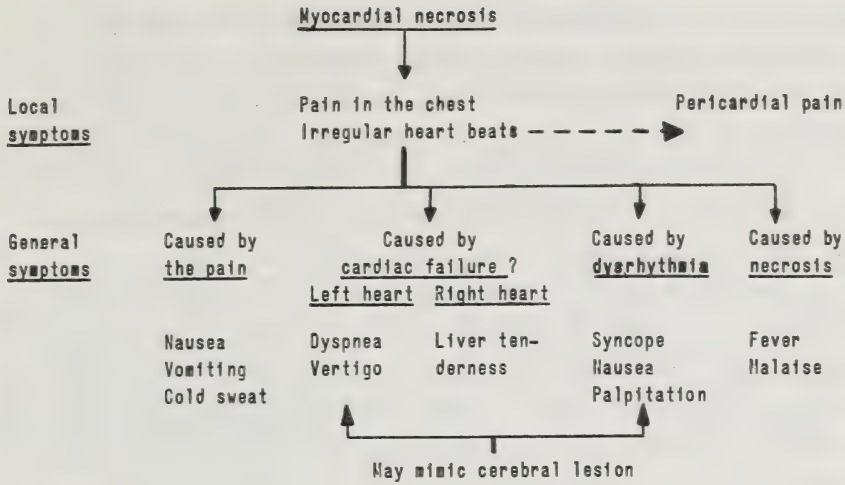


Fig. 14

Symptoms of myocardial infarction and their interrelation.

The precipitating event generally turns the life line downwards, for the time being or for ever. It exposes the state, to which predisposing factors have carried the patient, the life potential so far lost. All our life is a loss of potential - potentialities being used up and gone. If nothing befalls us, we will live for three scores and ten years (as stated in the Bible), or perhaps to a hundred or more. Death at a hundred years will probably be a cardiac death, perhaps of the "electric" variety.

With loss of potential, gradually evolving, or stepwise, or perhaps being there already from the beginning, inborn, as a kind of predestination, the safety margin, the homeostatic capacity, at any age will be less than "normal"; the vulnerability to precipitating factors greater.

Prevention, or postponement, of ischaemic heart disease must, in principle, be directed against three targets - the predisposing factors, the precipitating factors and the factors associated with the treatment of the acute event. Of these, the first and the last ones may be amenable to intervention. But can we really do anything to avoid the precipitating factors? Can the edge be taken off them? Can they be postponed? Let us have a look at them! Most infarcts appear to develop at home, in tranquility, at rest or during sleep (- but in that sleep what dreams may come?). Because of the unknown "incubation time", which may be a matter of seconds with malignant arrhythmias but perhaps a day, or more, with a thrombotic process, it is hard to tell which factors are really the precipitating ones. Perhaps one will have to resort to Hans Selye's concept of "the pathogenic situation" to get as close as possible to the truth. This, then, would allow for the inclusion of so-called "psycho-social" factors as precipitating agents, and it should be remembered that such factors, to use an expression by Sir George Pickering, mainly "operate through the mind". This, in turn, means that they may have no immediate connection with the actual social and personal situation - symbolic threats may appear and reappear in dreams or in anxiety with sources far back. Research reportedly being carried out by Bernhard Lown (98) along Pavlovian lines may render new information in this regard. Neither must there be one, singular precipitating event: the work of Holmes, Rahe and collaborators (54, 55), Theorell (52, 59) and others indicate the importance of a gradual build-up of "life changes" in the months preceeding an infarction - an opinion already held by Hippocrates (93). Then, however, we are in the borderlands where predisposing and precipitating factors meet.

Where have research and development taken us?

In a presentation twelve years ago, before the Swedish Society of Medical Sciences (72), I tried to define the goals in our work with ischaemic heart disease thus:

1. Postpone the occurrence of the first clinical event.
2. Reduce the acute mortality (e.g. in myocardial infarction and arrhythmia).
3. Delay the manifestation of serious recurrences.
4. Improve the after-care and rehabilitation.

I believe that, by now, we have been reasonably successful with regard to the goals 2 and 4, while not very much has been achieved with regard to goals 1 and 3. What could be accomplished in, or near, the hospital has been achieved, to a point. Activities in the community have hardly reached beyond the experimental stage.

Lessons from pharmacology.

With regard to drug treatment, prophylactic or therapeutic, there have been some major advances during these years. Specifically, one may mention lidocain and clofibrate - one Swedish and one British contribution to our arsenal - both of which have made a profound impact all over the world. In addition, high-powered diuretics and β -blocking agents (another British "first") have been of great value, the former in relieving hypertension and left heart failure, the latter ameliorating both angina and high blood pressure in many cases. Again, it can be stated, that developments geared to hospital medicine have been particularly successful, but in this case the effects have also penetrated into the community.

Lessons from intensive care (coronary care units).

The introduction of co-ordinated, intensive care for patients with suspected myocardial infarction in coronary care units has undoubtedly reduced the hospital mortality in this disease very considerably. Criticism and scepticism directed against this organization of treatment has been voiced in this country and elsewhere. It has been said, that the number of ischaemic heart disease-deaths that can be prevented inside the hospital is only a

small fraction of the many more deaths in acute heart attacks occurring outside the hospital. Coronary ambulance and mobile coronary care units have been answers to that question, but, of course, they are only partial answers. However, it is as far as one can reasonably go.

Three years ago, in this country, it was also argued that coronary care unit results were no better than home care. I do not believe that this is so, and I have not heard of any hospital closing its coronary care unit for this reason.

A more intriguing question has been, whether the improved survival rate of the coronary care unit patients would be maintained over the years. Data obtained by Hofvendahl (34) indicate that this is so, at least for the first five years, when randomly selected patients from our coronary care unit are compared with such as had to be cared for in our general wards.

Lessons from surgery.

After a rather long period of trial and error, with modest success, coronary surgery in the late 1960's, by the use of vein grafts, developed into a major medical industry in the U.S.A., probably already reaching into six-figure-numbers. Our experience is very limited. If the indications "intractable angina" and "pre-infarction angina" are applied, as we do, the number of candidates is small even in a large service. Altogether, over five years, perhaps two hundred patients have been operated on in Sweden, which, so far, means approximately five patients per million inhabitants per year. (An unproportionate number of these are said to be young Finnish workers!) An unbiased evaluation of the results from - and indications for - coronary surgery is urgently needed but very hard to perform, as a comparison with the pre-operative clinical condition is difficult and the subjective element in the improvement hard to avoid. But it is evident, that any measure that promises relief of suffering and hope of a prolongation of life is here to stay, at least for those who do not "rather bear those ills they have than fly to others that they know not of".

Lessons from epidemiology.

Not so long ago, my compatriots in Gothenburg (99) announced that 20 per cent of their fifty years old men were harbouring 3 risk factors and 8 per cent 5 such factors. To me this was a surprisingly high prevalence, but one that might make selective preventive measures worth while. To-day, from the same center (74, 80), follow-up studies have shown that a considerable number of "new" infarct cases derive from what were regarded as low-risk individuals, while a great number of high-risk individuals has not developed manifest disease between the ages 50 to 60. Tibblin (78) recently calculated that "to save" six persons by primary prevention, hypertension or hypercholesterolemia had to be treated in 200. Rahe and co-workers (79) have also remarked that even American figures show that 95 to 97 per cent of subjects with high risk factors do not develop myocardial infarction or coronary death the following year. They feel that better knowledge of precipitating factors might add considerably to the specificity of prediction. At the same time, it is apparent that many of the conventional - and new - risk factors are non-specific indices of increased morbidity and mortality from several causes, not only from ischaemic heart disease. Finally, an impression is gaining ground that the homogeneity of the ischaemic heart disease concept is withering, with a shift of emphasis from the obstructed coronary artery to the capricious and vulnerable myocardium, perhaps with different sets of pre-disposing and precipitating mechanisms. Thus the prerequisites for prevention (Fig. 15) such as I defined them in 1962 (72), have become less, rather than more comprehensible, and our ability to choose the right prophylactic regimen for the individual susceptible person may not have improved. We know more, but what we know makes things more complicated and less easy to handle.

Prerequisites for prevention

1. The mechanisms of the disease must be known and methods to interfere with them be available.
2. Simple methods to identify "susceptibles" must be available.
3. "Susceptibles" must be willing and able to change their mode of life, if necessary, (or to take "prophylactic" drugs).

Prevention of some diseases (mainly infections) is clearly feasible under the above conditions.

As regards some other diseases, with a multifactorial etiology, such as ischaemic heart disease, "prevention" is probably = postponement.

Fig. 15

Lessons from society's activities.

While medical men all over the world have been piling up arguments to prove that ischaemic heart disease is the "major epidemic" of our time and traced its origin back to many of the features of the Western civilization, our political leaders have remained fairly tranquil. A year ago, a WHO press release (3) stated that "this disease may therefore be an indicator of man's maladaptation to his civilization and may become an important factor limiting further technological and economic advance". Resolutions carried by international organizations as usual have been properly placed on the shelves of the national governments. Mainly for other reasons, viz. lung cancer, cigarette smoking has been condemned and some obstacles put on the sale of cigarettes, with little lasting effect, as far as I understand. Food industry, rather than agriculture as such, has developed various butter substitutes, but the total fat consumption in our populations may at best remain steady at a high level. If the sale of automobiles has suffered a certain drop, it is rather an effect of Arab politics than of the way our own governments handle the national economy, though the latter, unintentionally, still may contribute somewhat.

Ten years ago, in Manchester, I was asked to discuss "The next ten years in medicine" (100). In so doing, I remarked that "in the race with scientific and technical development social organization will always lag miles behind". I believe this still to be true. This is why I have repeatedly asked the question, whether there is any hope in remodelling our outer environment - society - or whether we must accept its follies and concentrate on the reinforcement of our inner environment - Claude Bernard's milieu intérieur - by pharmacological means and neurophysiological techniques (101, 102).

Aims and consequences of prevention

Intervention studies.

The real proof of what environmental factors contribute will come when the present "intervention" studies, that are being carried out in various countries, have made up their accounts. Such intervention studies have aimed both at reduction of specific factors, e.g. change of diet in "captive" populations (103), and at secondary prevention in survivors of myocardial infarction (104); others have tried to attack the problem by medication (41, 105, 106). In an attempt to provide experimental conditions in which due consideration is taken to "the real life situation in which health policies must be determined", the European branch of the WHO has set up a series of "multifactor preventive trials" in several European countries (51). This body of experts has agreed to the following order of priorities within the study:

1. Cholesterol lowering by dietary advice.
2. Control of smoking.
3. Control of blood pressure.
4. Increase of physical activity.
5. Decrease of overweight.

It was also stated that "extreme personality traits" were less common in Europe than in the U.S.A. and that no relation had been found between such traits and the risk factor score. Therefore, psychological factors should not be given prominence in preventive trials!

Only few results have as yet been reported. What is known speaks in favour of the feasibility of influencing certain biological factors and the number of episodes of clinical illness as well as the mortality spectrum. Some effects have been rather surprising: such as the reduction in numbers of death, mainly in patients with angina pectoris and regardless of the effect on hyperlipid states, in the British clofibrate study (106). So far, I know of no pharmacological reason for this. But it may well be that there is an interaction of biochemical factors, in the liver or in the myocardial cells, that is still hidden to us. Regardless of the deep levels of action, we know from the large multifactorial intervention in whole populations during World War II - involving i.a. dietary fat, cigarette smoking and physical activity in many countries including my own - that rapid and remarkable changes in mortality rates in fact took place (Fig. 16).

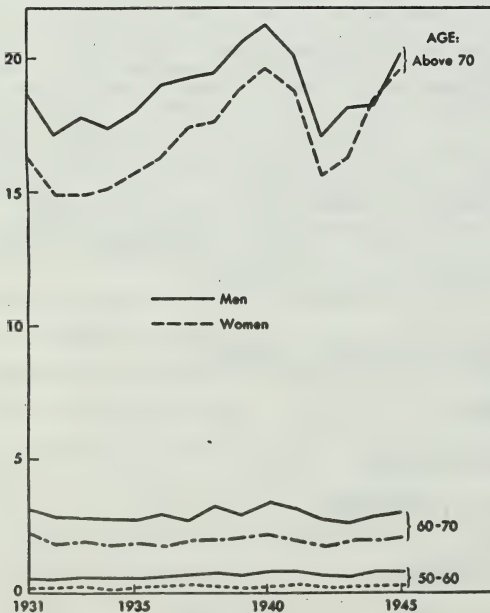


Fig. 16

Deaths from "arteriosclerosis" per 1.000 Swedish men/women, 50 years of age or more during the years 1931-1944.

It was after the return of the socio-economic conditions to levels regarded as more "normal" that the mortality trends rose again, sweeping with them partly also the individuals, in whom death was postponed during 1942-1944 (107). The further extension of this tendency, particularly in Norway, has been discussed in a very thought-provoking way by Westlund (108).

The natural course of disease.

In an attempt to illustrate the development of ischaemic heart disease over time I draw a horizontal picture (Fig. 11). I shall now try to present a different picture (Fig. 17), vertical for a change, in an attempt to illustrate the natural course of this disease so as to ask the question: when might what have been prevented?

The problem here is not only the "multifactorial" origin of the condition we call ischaemic heart disease, neither is it the variety of pathogenic situations to which all of us get exposed, nor is it the very long time course of the development of the disease process - probably from adolescence to retirement - but, as shown in this picture, it is the narrowing down of almost the whole population through the "susceptibles" to the individual patient and - in consequence - the question: can we apply what is epidemiological and clinical statistics to the individual patient (24)? How should we act to prevent a few cases of sudden death in the fifties or progressive cardiac failure in a great number of octogenarians? And in particular (71), how could we prevent sudden death at a younger age and promote it at a later?

Aging.

Much will depend upon research into the process of aging. More and more evidence seems to be collected that "premature" death from ischaemic heart disease may be conditioned by factors that promote premature aging and the untimely breakdown of various bodily processes, not only those of the circulation (7, 73, 109,

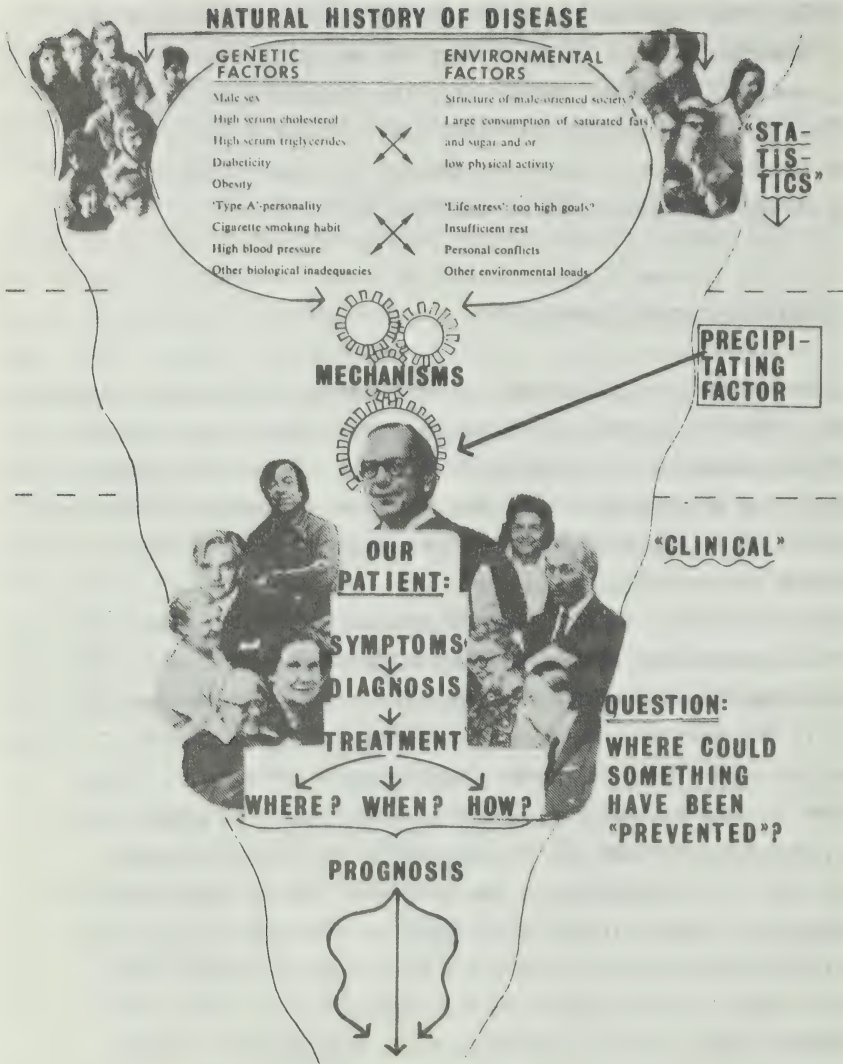


Fig. 17

110, 111). In many prognostic studies, age does appear as a very important factor. To me it is evident that more research should be directed to the understanding of factors, from within and from without, that determine and influence the process of aging (82, 102).

"Premature death" and prolongation of life.

From society's point of view, there are other problems than those of reducing alleged environmental risk factors. Of even greater importance is the balance between, on the one hand, "premature deaths" and, on the other, its counterpart: the prolongation of life in the upper age groups.

Maurice Campbell (112), in 1963, maintained that "all the large increase in deaths from heart disease since 1920, including coronary heart disease, can be explained" by the fact that one quarter of those whose lives were saved from premature death in infectious diseases and tuberculosis "subsequently died from heart disease at the ages when other persons die from this". Campbell also predicted that the increase in coronary deaths in England should level off to be "almost steady by 1977 and completely so by 1990". This is a daring prediction and we will look forward to the midpoint of Campbell's chosen years which is 1984.

Now, what is "premature death" in our time? Don Fredrickson - the President of the American Institute of Medicine - once defined this as death before age 66 (113). This is a little more than the sixty years of age that William Osler considered as the end of usefulness and a proper time to withdraw, in his valedictorian address in Baltimore (114). From this point of view, the deaths of the Earl of Clarendon in 1674, at the age of 65, as described by his son, and of John Hunter 1793, in his 65th year, must be considered right in target (115).

Many international statistics seem to end with the age group 60-64, totally disregarding anything above that as "illdefined" and I suppose, presumably useless. As you have seen earlier, in my country, 80 per cent of the male ischaemic heart disease mortality and probably about 65-70 per cent of male ischaemic heart disease morbidity occur above that age. For England and Wales, the

corresponding figures are 70 and, perhaps, 55 per cent. People, who are thinking in concepts of the economy of production often calculate astronomical figures of loss of earnings and production for the middle age groups. The economy of consumption as concerns the older age groups is rarely mentioned (116).

Preventive medicine and "natural death".

The more successful medicine - including preventive medicine - is, the more people will survive to old age. Up to the present time old age, in a great number of instances, has carried with it an accumulation of disorders, diseases and disabilities, which - together with isolation, reduced financial resources, faulty memory, loss of purpose, and similar limitations - has led to an ever increasing demand for institutions for custodial care.

The gradual move from a three-generation society to a four- or even five-generation society is apt to create increasing strain between the "productive" (and reproductive) generations and those who will mainly be at the receiving end. Those citizens who are now in their fifties or sixties are probably carrying more burdens than any other generation heretofore. Not only did they become parents at a time when the "child's century" was proclaimed and had to negotiate their conditions with a spoiled generation, but after this was over, they had to divide their time between outside work, babysitting for their grandchildren and care of their own debilitated parents all at the same time. It is perhaps no wonder that their children, now entering the adult world and finally facing their responsibilities, are the ones who, in anticipation, are raising the questions of the meaningfulness of a long life and are among the ardent spokesmen for euthanasia.

At the same time it appears as if the industrial society - we have not seen any "postindustrial" society as yet, and it is not so certain that it will ever materialize - is not capable of finding enough jobs for its citizens, at least not jobs that are economically meaningful in terms of net profit, or at such salary levels as are deemed acceptable by society and labour. In such a situation the pensioner may find himself with many "years to life", and probably a good deal of "life to years", but nothing really to do, until,

in due time, general tiredness, weakness and lassitude overtake him and his horizons shrink. Eventually he may then succumb to what a professor of geriatrics has labelled a "natural death".

Not only governments and medical administrators have expressed their concern about this development. The no-longer-so-young generation has also observed the writing on the wall. In an enquiry to a fair number of Swedes over the last few years by one of our weekly magazines, one of the questions was: How do you want to die? A very big majority, particularly among the males, indicated that they were hoping to pass away rapidly and without warning (71). What cardiologists all over the world rally to prevent appears to be precisely what many of those "at risk" seem to prefer.

Yesterday, at Oxford, I asked the question whether ischaemic heart diseases is a "medical" or "psycho-social" disorder. In another address, (102), some years ago, I ventured the question whether it were to be regarded as a "disease" or "a way of life and a mode of death".

Those of us who have been caring for old people know that, in some cases, there are hearts which - with a popular phrase - are too good to die even in a situation where almost all other organ systems are disintegrating or on the road to collapse. There are people in whom, at the end, it is to be regretted that they always has such a strong heart.

How to influence the causes of ischaemic heart disease?

Twenty years ago, when the great epidemiologic campaign started, it was felt that identification of risk factors might provide clear-cut arguments for medical intervention in the "causes" of the new Western epidemic of heart attacks. To-day, very little has been achieved in this regard, practically. The problems either are less clear-cut than we believed, or we have managed to cloud the view by all sorts of irrelevant speculations, as I may be accused of having accomplished here. In all circumstances, however, the task of translating medical opinions into political action is enormous. Information and health education

are good things, but so far, have not shown themselves to be very powerful in motivating people's behaviour. Changes in food habits and in the use of such mood modifiers as cigarette smoking are economical problems, charged with much emotional tension, if nothing else. Political action in these areas goes far beyond the realm of Elephant and Castle. One of your more spectacular Ministers of Health wrote a book, in which he maintained that the only thing such a person ought to discuss with the medical profession was money (117). If he had ventured an attack on ischaemic heart disease, he would have had to turn elsewhere to discuss economy.

How do statesmen reason, and what kind of information do they need to do it?

The brief survey I have given over various problem areas in ischaemic heart disease has served mainly to provide material for answering some hypothetical questions, that would possibly be raised by statesmen if and when we approach them to ask their assistance. I shall now, finally, try to answer the question raised by the title of this paper. But first of all it might be useful to ask another question: Why are we supposed to address our statesmen? Why not stick to our own job and leave theirs to them? After all, we are physicians, not politicians.

There are at least two answers to this. One is that in both our countries, with the introduction of compulsory health insurance systems, politicians and professional administrators have made themselves our masters, and the spokesmen of medicine have not been successful in promoting its case in the corridors of power. The corridors of power that we control are those in the wards, and these are among the few places where occasionally even a minister is willing to consider seriously our arguments. That is why I believe that clinicians have a better chance than public health people to influence many developments in society, provided they are sufficiently knowledgeable and well-oriented in issues of general political significance. This opportunity is - sometimes for reasons of professional ethics, but sometimes only because of ignorance - not always grasped.

The other answer - and this is the main one - of course, is that many of the proposals that have been advanced by medical men in the scientific debate concerning ischaemic heart disease do need society's money and machinery for their implementation. Now, where are the limits between what we can do ourselves and what we cannot do without society's machinery?

"Pilot studies" with regard to screening procedures, rehabilitation programs and even "intervention" programs may be conducted by ourselves within existing organizational frames and with the financial support from research grants. But whenever such pilot studies are to be transferred into full scale undertakings, this has to be handled by society (or, in some cases, e.g. industry). If such "environmental" factors as the chemical composition of tap water, or that of nutritional fats, were to be controlled, or manipulated, this would have to take place by persuasion of the producers and/or by legislation. The same thing holds true of any interference with cigarette smoking. If heavy consumption of alcohol will turn out to be the most prominent "secondary" risk factor in other countries to the same extent as in Gothenburg, Sweden, (78), then this definitely is a tremendous challenge that, so far, no government has succeeded to tackle.

Here is an interesting duality: the interaction of information and persuasion, on the one hand, and political action on the other.

Particularly in situations, where considerable resistance against a political decision is to be anticipated, politicians are apt to demand organized public support - originating at the grass-roots - for the action to be taken before they begin their own moves. Even though they may well see the rationality of a proposal, they prefer to act in response to what appears to be a public demand. My feeling is that little effective action will be taken in the health area, unless it can be recognized in the form of a public demand. Many years ago, when I discussed the expansion of governmental support for medical research with our then Prime Minister, Mr. Erlander, his advice was for us to go out and tell the public and ask them to put pressure on the government for more money for science (Fig. 18).

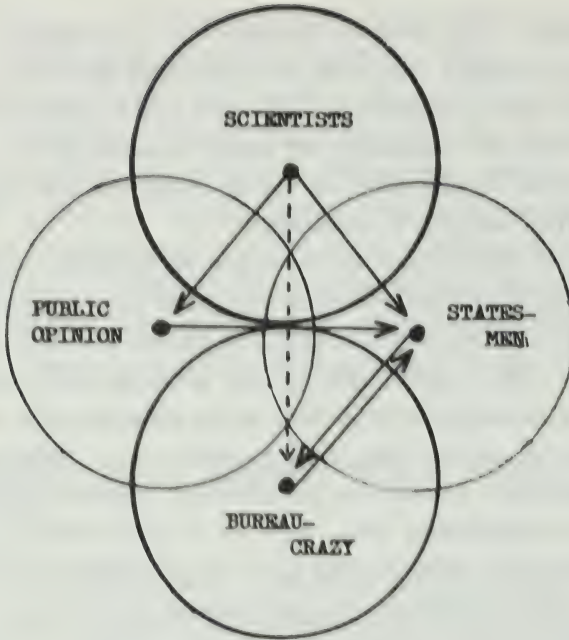


Fig. 18

Four sets of power.

This is a cumbersome undertaking, and not a very familiar one to doctors, but it is precisely what the "organization men" and the manipulators of our mass media are used to devote their time and their techniques to. One of the problems with the illumination of the public is that it has to be one-sided, dogmatic - biased if you so prefer - and that it has to be carried with conviction and enthusiasm, if it is at all to be heard above the general noise-level. This is against medical scientific upbringing and professional rules. Not many medical men are terribly keen to preach the gospel. In particular not, if they are none too sure about what the gospel is. Among the worst things that can happen in health education is the preaching of several, different gospels at the same time.

For this reason, and against the background of my previous discussion, I am worried about some public statements such as the one reported from a WHO conference in Brussels a year ago (2):

"In affluent societies ischaemic heart disease is the most important single cause of premature death and disability among men at an age when their contribution to society is most valuable. - The control of ischaemic heart disease is therefore the most important task in the community. - Governments were asked to make provision for the implementation of the recommendations presented by the Conference. Such recommendations were: The community as a whole should be approached and helped to change the modern way of living as such. Influence the adverse dietary habits of the populations. Citizens should have the right to live in an environment unpoluted by tobacco smoke. Emphasis should be placed on physical education throughout life."

It is difficult to see, how one can maintain, on the one hand, that "the etiology of atherosclerosis and ischaemic heart disease is still unknown", and, on the other, that "the community as a whole should be approached and helped to change the modern way of living as such". Similar thoughts were also expressed in a motion to the Swedish Parliament by the Center Party last year (1): "Modern diseases like ulcer, asthma, goiter, hypertension and myocardial infarction have greatly a psychosocial etiology. They are often psychosomatic. One third of 60-70 million days of sickness are caused by stress and insecurity. This is also true of disability pensioning and of the abuse of alcohol and narcotics."

Such, after more than twenty years scientific research into the pathophysiological mechanisms of atherosclerosis and ischaemic heart disease, reads a qualified interpretation by politicians for politicians. Is this, after all, all that is needed?

Professor Morris, in an address two years ago in the Royal Society of Medicine (93), found himself in a similar quandry. Having stated that "the question is one for judgement in face of inconclusive data", he went on to ask: "How can we influence the social pattern and prevalent life styles and shift norms of behaviour? That is far the best way, and, if we cannot, we are likely to fail also with high risk groups and vulnerable

individuals; all three certainly have to be confronted at the same time. The agonizing question is how, when popular behaviour is changing so fast and so often, how can we encourage it towards better health?" I shall not discuss the very simple rules of life that he advocated. They are based more upon experience and common sense than on refined medical research. But I shall emphasize the words "can we influence", "can we encourage", etc. Who are the "we" supposed to prescribe shifts in the norms of our compatriots' behaviour? There can be given strong answers to such a question. But we must be prepared that it can be raised - and will be raised - in any democracy, where many pride themselves on having swept aside the authorities.

Yet, there is obviously a rising demand for something to be done:

Congress Urged to Raise Spending to Cut Heart Toll

WASHINGTON, July 28.—The long-awaited report to Congress on diseases of the heart, circulatory system and lungs recommends sharp increases in research funding with strong emphasis on studies of arteriosclerosis as the underlying villain in the nation's foremost health problem.

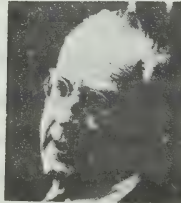
The document is really a national five-year plan for combating the problem. It recommends spending \$46-million more this year than is called for in the President's budget to support operations of the National Heart and Lung Institute. It says that the high American death rate from heart disease is neither necessary nor inevitable.

In letters of transmittal to both houses of Congress, Frank Carlucci, Under Secretary of Health, Education and Welfare, criticized the report on the ground that it did not consider the needs of heart research in relation to the full spectrum of biomedical research.

"Since cigarette smoking has been demonstrated to be an important risk factor in arteriosclerotic heart disease, all smokers should be urged to stop."

Such declarations are flabby indeed.

The feasibility of public educational campaigns is discussed. Such campaigns are important but first it is desirable to have something to communicate.



"Was this really necessary?"

Need for work, not talk

Irvine H. Page, M.D.
Editor

Fig. 19

Some strong feelings.

If this be so, I think we will have to turn to our statesmen to do whatever needs to be done.

Decisionmaking

The task of statesmen is decisionmaking. This is also the task of physicians, by the way, although few physicians actually conceive of themselves in that capacity. (More is, however, being learnt about this in recent times, and a conference on the subject will take place in this College in a near future.) Both politicians and physicians prefer to make decisions on the basis of substantial and non-controversial evidence. More often, however, they will both have to decide on meager and conflicting evidence. In matters of public health, politicians are accustomed to seek information and advice from the bureaucracy at their disposal rather than from medical sources. In many places, I believe it is fair to state that the bureaucracy in reality manipulates the politicians, and this is particularly true, when there is a rapid turnover among those who hold the political offices. Therefore it is all the more important that physicians make their way to the politicians directly so as to influence their reasoning. Reasoning, according to the Oxford dictionary, is defined as "form or try to reach conclusions by connected thought silent or expressed". It will, then, be necessary for us to translate our concepts into the kind of concept they are accustomed to work with in order to elicit action. It is doubtful, whether it is wise to tell any decisionmaker how to act. But enough facts should be presented so as to make action almost selfevident, yet being conceived of as an original idea by the decisionmaker himself.

Occasionally, however, the decisionmaker is an original thinker himself, and this is the one we have defined as a Statesman. Rather than being fed prefabricated concepts by administrators or by ourselves, he is the one who takes the initiative in asking questions. We must be prepared to answer them.

A statesman thinks aloud.

Statesmen are often interested in figures. So our statesmen might ask us: How do you explain the difference in mortality - and presumably morbidity - rates from ischaemic heart disease between England, Sweden and Finland? Is there really anything in the mode of life, or environmental circumstances, here in England that can be made responsible for our excess deaths in comparison with your figures? If ischaemic heart disease is a disease of the Western civilization - then, are the British more civilized than the Swedes? Do we smoke more cigarettes, is the air more polluted, are our pubs and the Finnish sauna-baths conducive to ill health? Or, is it that the anxiety caused by fear of economic insecurity is better handled in Sweden than in countries like ours and, particularly the U.S.A., where mortality from ischaemic heart disease is said to correlate to economic crises (118)? Or, are we now witnessing the long-term effects of the second World War in England and Finland, but less so in the neutral Sweden? Do we have answers to that?

Statesmen are lay people: they like to connect hard facts in a simple cause-and-effect way. They might ask us: this process of atherosclerosis and of coronary artery thrombosis - is this a specific disease or just one feature of the process of aging, whether "premature" or not? There was one time, when it was said to be a result of the aging process; then came a time when this was vigorously disputed and it was said to be a specific disease which could be prevented - now, it appears, the pendulum is swinging back towards the process of aging, but at the same time this very process is being divided into "normal" and "premature", and one is back to the question of the general biological clockwork, and to a more subtle concept of the interaction of genetics and environment.

I guess that some of our statesmen may be irritated by this degree of sophistication and switch the discussion back to practicalities. Then, they may ask: How certain are you that present knowledge is definite, the final word, more or less? And they may - if they are properly briefed by their undersecretaries

- remind us: didn't you at one time say that animal fat was dangerous and vegetable fat good? - Yes, some of us did. - And then you said that saturated fat was bad, and unsaturated good? - Yes, we have said that. - And then, in some countries, you made margarine from rape-seed-oil which contained erucic acid, which is bad for the heart? - Yes, this happened, but it wasn't probably too dangerous in man. - But you had to finish this practice, nevertheless? - Yes, we felt this was the proper thing to do. - And can you assure me that no other, similar troubles will occur, if we shift peoples' diet by governmental decrees? - No, we cannot foresee everything. - And is there not a fellow who puts the blame on sugar instead? - Yes, sir, there is. - And do not carbohydrates and alcohol change your triglyceride levels and move you out and in between types IV and V? - Yes, they may, but this is not so important. - Only protein, then, seems to be innocent. But meat is expensive, and will become even more so. Frankly, I do not think governments should interfere with peoples' food habits. There must be some freedom left, after all.

- After which our statesman lights his cigarette, stating: I know you think this is dangerous. But I don't believe that, I need it, to cope with the day-to-day charges, and I am not going to finish. That takes care of that. While inhaling, he ponders over prevention and the electorate:

-What do people really want? To live longer or to live well while they live? I suppose that depends on how old they are and how old they are likely to get. The younger they are when they get sick, the greater is the likelihood that they are willing to buy a prescription for a longer life. In this respect, the preventive aspect seems to carry greater weight in England and in Finland than in Sweden. In Sweden, I understand that even former proponents of "primary prevention" are getting less enthusiastic and are rather more inclined to emphasize "secondary prevention" - of those already sick. But in England there might still be a case for straightforward primary prevention. If this will be good national economy or not nobody would care, until too late, anyhow. But few may be willing to make any sacrifice themselves.

It has been said of the war years, in some countries, that dietary restrictions, and other similar setbacks, improved the health of the people. Maybe, in this country a regimen of restrictions could be presented to the electorate as a regimen of health? Maybe this is how a medical proposition could be turned into a political issue? Economic necessity, thus, would satisfy a humanitarian purpose. Not bad, indeed. Yes, I think this might well be a political question. Or it could be made one. Gentlemen, I thank you for having assisted me so well in my forward thinking.

By the way, I have myself experienced a funny feeling in the chest, for some time. I don't think it is really anything serious. But perhaps I could have a check-up made. Or should I not? What is the best, to know or not to know? What do I want with my own life? To live on, or to accomplish what I have set before me? To continue, regardless of consequences, or to try to avoid consequences even at the price of resigning from duty? Unfortunately, gentlemen, this question is up to me to answer, not to you. I am perhaps not so young any longer. I have always envied those who pass away unknowingly. Maybe one should be cautious in looking into the chrystal ball, oneself? Health may be a goal for the public, but not necessarily for those who serve it in office.

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DIETARY HABITS AND THEIR BACKGROUND IN A SWEDISH POPULATION GROUP ¹

(By Professor Gunnar Biörck, M.D., Rune Persson, Ph. D., and Björn Nystrand, Assistant)

The technical and medical development has brought about a continuous change in the population development within our culture. This change is related to a decrease in child mortality, early middle age mortality as well as to an increased average life span. In this connection, cardiovascular disease and its death rate have come into the foreground. This group of diseases now tops the list of causes of death in our part of the world.

There are many opinions whether the increase in cardio-vascular disease, which has statistically been proven, is comparable to an equally great increase during earlier periods.

However, it is obvious that the problem, regardless of whether there is a real increase or not, is so great and so serious, that one has to ask: Must the disease and the mortality rate be so wide-spread? Have we done everything we can in order to stop it? Can we be satisfied with the way it is?

The answer to these questions can only be: *No*. One of the reasons is that the occurrence of cardio-vascular disease shows actual differences both between different population groups and within the same population group. Through extensive, international work, initiated and directed by the American professor Ancel Keys, and in which one of us (G. B.) had the opportunity to participate, material has been gathered from various sources and by using a number of methods. This material points out the differences.

Thus, it is difficult, if not impossible, to forego the conclusion, that even though the more complicated mechanisms behind arteriosclerosis of the heart and the vascular system are not yet fully understood, many contributing factors can be shown, which seem to have an effect on the extent of the disease in question.

One could, of course, devote one's attention to factors such as race, heredity, sex, climate, diet, physical and mental activity. Several such studies have been carried out and are still being made. When Keys and his group directed their attention especially to the questions of diet, it was for four reasons. One thing we know is that differences in the disease pattern and mortality rate can be observed in groups of people with different diets. The frequency of arteriosclerosis is, for instance, lower in Italy than in the United States and Sweden. One of the differences is the diet, especially with regard to the fat contents. Another well-known fact is the decline in the mortality rate in general, and also with regard to cardio-vascular disease, which occurred in con-

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nection with the food rationing during the second World War in our country as well as in many other countries. However, a comparable decline was not noticeable in, for instance, the United States, where there was no food rationing to speak about.

Another reason for studying the diet is that the diet is the one thing among all the itemized factors that can be studied the most precisely. The last, but not the least important thing is, of course, that *if* it turns out that the diet is of any importance at all, it is one of the very few factors—maybe the only one—where it is possible to make a measurable, positive effort.

It should, however, be emphasized that it is possible to look for the importance of the diet with regard to the cause of arteriosclerosis without being single-minded. One should not expect an improvement in the diet to solve all problems but it is likely that such an improvement could decrease the spread of these diseases; furthermore, the diet is one of the relatively few generally effective measures which could be taken and could be useful also from other points of view.

We are well aware of the fact that different, often contradictory, advice has been given to the general public during the years with regard to diet. This has many times led to confusion, doubt and skepticism. This attitude probably reflects, to a certain extent, the attitude of the doctors in our country with the exception of the pediatricians. In this regard the situation in our country and the situation in the United States differ in many ways. In the United States there is still great interest in the diet in spite of the high standard of living. It can certainly be said that the present nutritional problem is the global question: "Is there enough food for all of us?" In this situation when there are food shortages in many parts of the world the question of detailed nutritional balance in the households of the well-to-do people may seem inconsequential. However, over-eating is almost as serious a health problem in the developed countries as inadequate nutrition in the underdeveloped nations. In addition, cutting down on over-eating would make food available to the underdeveloped countries where it is greatly needed.

It is well known that the least economical use of a certain agricultural area, with regard to nutritional value, is to keep livestock, that is, to produce meat and dairy products. Many more people can be fed if vegetables and cereals are produced instead, so that people can eat them directly without letting them go through the cow, the pig or the chicken.

The present trend in western society, like in the United States or Sweden, is that the total calorie consumption increases insignificantly or not at all—because it is already very high—whereas the percentage of fat out of the total number of calories is steadily on the rise. In Italy there is approximately 20 percent fat per total number of calories whereas in Sweden the fat percentage is close to 40 percent and in the United States it is almost over 40 percent.

There are fairly good scientific reasons to believe that the fat content of the diet may have something to do with arteriosclerosis. In tests the serum cholesterol contents were much higher in healthy Americans and Swedes than in Italians in comparable job categories and age groups. Such tests were performed last year by Keys' research team using uniform methods. A striking parallel between the fat content of the

diet and the occurrence of coronary disease in hospital patients was also noted (Figure 1). Animal experiments² seem to indicate that a diet containing a lot of fat shortens the lifespan, whereas a certain moderation in the diet during certain periods of one's life seems to be beneficial.

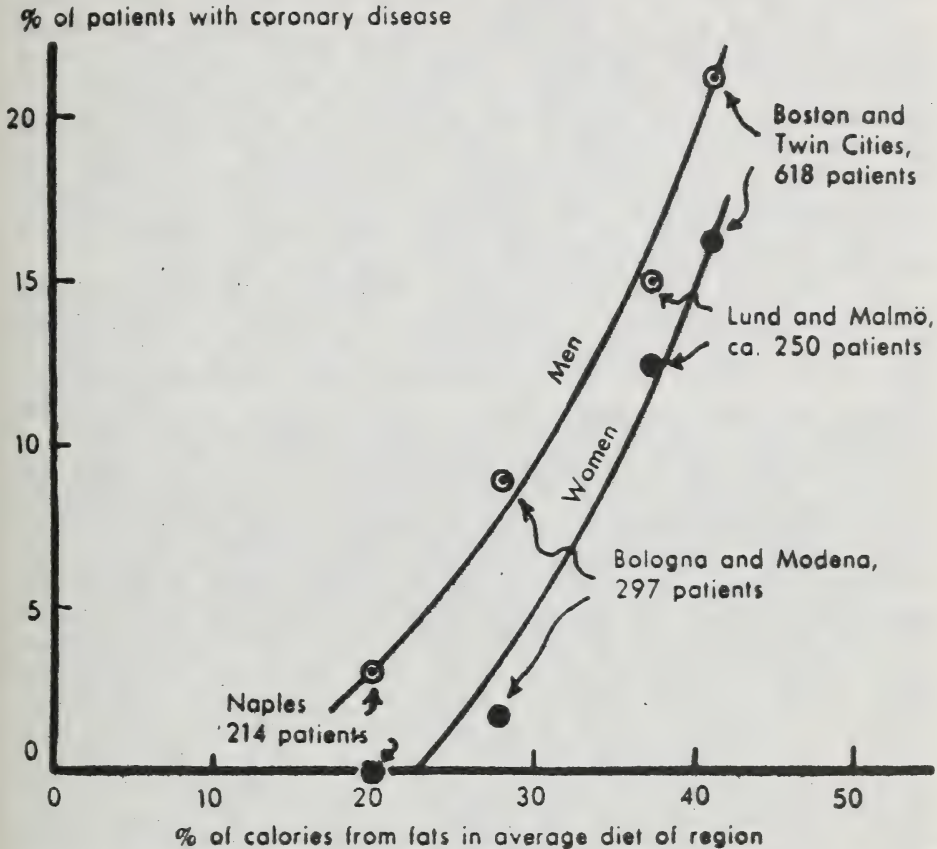


FIGURE 1.—The relationship between the percentage of hospital patients with coronary disease and the fat contents of the diet in certain cities according to E. Klepetar.

It is obvious that there are many substances in the food and that one should not only look at one detail. But if there is a certain systematic change in the diet of a people and, above all, if one can suspect that this change may cause some harm, then there is a good reason to study this change more closely and to ask what kind of measures it may possibly bring about. It is then possible that one should try to come up with another type of diet, a more "balanced" diet, to use an American expression.

In Sweden there have been extensive studies of the diets and the households on several occasions. These studies, however, were intended in general to show the actual situation rather than to look for the motive behind the choice of diet. The less diversified the economic system is in a country and the poorer its population, the more import-

² M. Silverberg, R. Silverberg: *Diet and Life Span*. *Physiol. Rev.* 35, 347, 1955.

ant the present availability of food and the economic necessity are to the choice of food.³ In the situation that the Swedish population of today finds itself, one has reason to believe that both these factors will become less important in comparison to other factors. If the freedom of choice increases, more diversified motives will become obvious. It may then be interesting to study these motives more closely and to find out why we eat what we eat. In a situation where there is a fair amount of freedom of choice, such as the one at the present time, it is obvious that a conscious change in the eating habits of the population is only possible if one considers the motives determining the actions of each individual. This concerns both the heavy artillery of the food industry, the barrage of the food sections in newspapers and magazines and the weak whispers from activities of the medical community, which in the Anglo-Saxon countries are called "health education", but which in Sweden have very little influence.

An American study⁴ of the motives influencing the choice of food started the collaboration, of which these are the first results. Through this collaboration a significant approach to the problem with regard to preventive medicine has been undertaken using sociological methods. Maybe the most remarkable data in Lewin's paper was that, in his American test cases, the health aspect of the food was found to be of very high priority. In the upper socio-economic group this aspect was the most important one, in the middle group it followed closely the economical aspect and in no group was taste the most important factor even though it was more important than the price in the upper socio-economic group. The importance of the health aspect as well as the non-importance of the tastiness seemed unusual. One of the reasons for the importance of the health aspect could, however, have something to do with the intensive advertising put on by the American food industry, which advertizes the health aspects to a great extent. What is a primary reason or an adaptation to the consumers' likes and dislikes is impossible for us to determine. In any case it seemed that it would be very interesting to study what the food habits and the motives behind them look like today in a Swedish urban population. Thus communication was established between the departments of Medicine and Sociology at Lund University.

Such a general survey should also help make consequent studies with more specific objectives easier. It is obvious that if one wishes to make predictions about the possible effect of certain sociological or other measures in order to change the direction of consumption, a special study should be planned more as an experiment. Such an experiment could, however, hardly be undertaken without access to basic data of the kind which this study intends to give.

THE PLANNING OF THE STUDY⁵

One ought to be able to assume that food habits vary between different parts of the country. For this reason we chose a city in Skåne, Trelleborg, and a city in the middle of Sweden, Lidköping. These cities

³ Certain aspects of this are touched upon by Wold and Jureen in *H. Wold: Demand Analysis*, Stockholm, 1952.

⁴ K. Lewin: *Forces Behind Food Habits and Methods of Change*. Nat. Research Council Bulletin 108, 1943.

⁵ The Study was made possible by a grant from the Marabou Co.

are similar with regard to the following aspects: size, number of labor union members, number of members of the co-operative organization, local assessment, availability of fresh fish. In addition, the two cities have a high school, a hospital and neither one has any army base. They each have a big industrial plant: Gummifabriken (rubber factory) in Trelleborg and Rörstrand (china factory) in Lidköping. Both are commercial centers in rather vast rural areas.

In order to study the variances between the socio-economic groups, the families in the study were selected in such a way that there was an equally large number of families from the three socio-economic groups (mainly classified according to the occupational grouping of the election statistics). Within each socio-economic group the selection was made in such a way that half of the housewives were working outside the home and half of them were not. Only housewives between the ages of 20-55 were included in the study and only families with children at home under 16. The selection was made at random from the voter registry and the data was obtained through personal interviews conducted by nine trained interviewers, who had been especially trained and who had then conducted test interviews which were reviewed.

The form used was the result of two preliminary tests using 65 families. The form had been revised as a result of these preliminary tests. The interviews were conducted between May 2 and May 18, 1955.

Major efforts were made in order to obtain as typical material as possible and therefore keep the number of people who refused to participate as low as possible, which one might say was achieved since the number of people who refused was as low as barely 2 percent.

The form contained questions about the consumption of certain food items, meat, fish, butter, etc., as well as questions which were intended to give a picture of the person's attitude and opinion of certain food items. Some of these answers were to be classified by the interviewer as taste, price tradition, health and convenience aspects of the food items in question. This table has been used previously by Lewin except for the last factor, convenience, which we added especially because of some of the processed, and above all frozen food products available today. During the review of the test it also became obvious that it would have been appropriate to distinguish yet another factor, that is the desire for variety. The form also had room for a weekly menu where the interviewer was supposed to report on what the family had eaten during the past seven days. The preliminary tests had shown that it was quite possible to reconstruct such a menu with a high degree of accuracy.

THE RESULTS OF THE STUDY ⁶

DIFFERENCES BETWEEN THE SOCIO-ECONOMIC CLASSES

In the tables to follow only the average consumption is usually given. It should be noted that the averages are based on the total number of individuals in each group, and not only on those who use the food item in question.

⁶A more detailed presentation of the study and the methods used are given in R. Persson-B. Nystrand. "A Study of the Food Habits in Two Swedish Cities". Lund 1955 (stencil).

As tables 2-5 indicate, the differences between the socio-economic groups can be summarized as follows: Socio-economic group III eats more butter, more meat (with the exception of veal and poultry), more sugar, more potatoes and more bread (with the exception of white bread and hardtack). Socio-economic group I eats more fish (but less herring), more organ meats, more vegetables and fruit.

Butter-margarine.—The results indicate that socio-economic group III consumes more butter than margarine. This is probably related to the fact that this group consumes more sandwiches (cf. the bread consumption), but it is also possible that there is a greater resistance in this group to using margarine than there is in socio-economic group I. All in all, socio-economic group I uses more margarine than butter, socio-economic group III more butter than margarine.

Bread.—The fact that so little white bread is consumed by socio-economic group III in Lidköping, so little hardtack by the same socio-economic group in Trelleborg, is probably due to tradition. Earlier, hardtack was mostly eaten further north, white bread mostly in the south. Socio-economic group III thus appears to be more bound by these traditions than socio-economic group I.

Meat.—The differences between the various kinds of meat seem natural, since the more expensive kinds are mostly used by the higher socio-economic groups. But maybe the explanation is not to be found only in the price. We will return to this later. Socio-economic group III eats, all in all, considerably more meat than the other socio-economic groups.

Fish.—Herring is the most predominant in socio-economic group III, whereas other fish is mostly eaten by socio-economic group I. If one combines herring and other fish one gets a somewhat smaller difference in the consumption of fish between these two socio-economic groups. However, if one leaves out the herring the difference is quite big.

Fruit.—The consumption of fruit was surprisingly high in all the socio-economic groups. The interviewers, however, were under the impression that the information given to them was accurate.

Vegetables.—With regard to vegetables, quoting the average frequency would be quite misleading since some of the people interviewed, only use certain vegetables during a certain part of the year. Therefore, the distribution is indicated instead, and the number of people who are non-users. In order to give an idea of the differences in the seasonal use, table 5a shows the differences in this regard between socio-economic group I and socio-economic group III.

As shown, there is a certain difference between the groups. However, the group which is indicated to be a seasonal user is far from uniform. It includes those who do not use vegetables at all other than seasonally, as well as those who have a marked consumption difference between seasonal and non-seasonal use. In addition, the data is in itself relatively unreliable. The interviewers found this question to be one of the most difficult to answer truthfully. In spite of the efforts there are probably several inaccuracies in the material with regard to this question. The figures should therefore rather be interpreted as a trend,

that is, socio-economic group I is less dependent on the seasons than socio-economic group III.

All vegetables are used the most by socio-economic group I, the least by socio-economic group III.

THE ATTITUDE TOWARD VARIOUS FOOD ITEMS

Meat.—Table 6 shows that the taste aspect completely dominated with regard to meat. The need for variety is also quite prevalent. The meaning of this factor is not quite clear. There are probably elements of both taste and health aspects but, in addition, variety is probably sometimes an answer that has been given instead of "yes, sometime or another one should have it", that is, a traditional answer. The price as well as convenience are mentioned to a certain extent with regard to pork, for which also tradition sometimes is given, mostly in socio-economic group III. It ought to be pointed out first that the category "tradition" has been marked only when the housewife has expressively said: "We have gotten used to it", "We have always had that on Sundays", etc. The few instances this category is marked should not be taken as an indication of how essential tradition in a larger sense may be. There are strong reasons to believe that habit as far as certain kinds of food are concerned is of much greater importance than what is indicated by these figures.

The differences between the socio-economic groups can be summarized as follows: Socio-economic group III indicates variety more often for beef, group I more often taste; group III more often indicates tradition and taste for pork, group I more often convenience.

If one looks at the total figures for meat one can see that socio-economic groups I and II more often emphasize the health aspect. In the specified answers it is noted that, with regard to pork, it is easy to prepare, it is juicy and it is well liked. "Just stick it in the oven and you have a nice piece of meat." (IH Tg)

As far as beef is concerned⁷ more emphasis is put on variety, especially when more elegant food is wanted. Many complain that it is dry. They also remark that it is low in calories:

"When you want something more elegant." (IH Lg)

"Low in calories." (IIF Tg)

"Too dry for my taste." (IIF Tg)

As to veal the health aspect is often mentioned, that it is low in calories, that it is low in fat, that it is good for children, for the stomach, and so forth.

"It is so good for you, so once in a while we try to have it, but it is hard to find." (II Tg)

Fish.—As far as fish is concerned mostly the taste aspect is emphasized, and to a certain extent also the price. As far as frozen fish is concerned the convenience aspect is more often mentioned.

Vegetables.—As table 8 shows the taste and health aspects dominate with regard to vegetables. The health aspect is especially emphasized

⁷ Different cuts and quality are probably selected from this kind of meat and the meat is probably prepared differently.

by socio-economic group I. Price and, even more, tradition, are mentioned somewhat more often by socio-economic group III. The differences between the vegetables are quite insignificant. However, the health aspect is mentioned somewhat more often with regard to tomatoes and cucumbers but price and tradition less often than for other vegetables.

Among the more specific statements it is also pointed out that the children must have vegetables because vegetables are good for them. Sometimes a wish for weight loss is also a factor. Especially in socio-economic group III, vegetables are commonly used in soups whereas socio-economic group I more often seems to use the vegetables "au naturel."

"The children need them and my husband is afraid of getting fat."

SUMMARY

With regard to both meat, fish and vegetables socio-economic group I indicates health aspects more often than socio-economic group III whereas group III more often indicates tradition and maybe somewhat more often price. However, price and tradition are very seldom mentioned. Tradition seems to be a factor that the person who is interviewed uses as a last resort. The interviewers had been instructed not to pressure the people they interviewed for answers but to note the spontaneous answers. The reason was that one is more apt to get a truthful answer if the answer is spontaneous. However, it is obvious that, by using this method, one finds that there is a very small number that will spontaneously mention tradition, which in reality plays a very big role. Therefore, one has to interpret this factor carefully. The price factor should, however, give a more direct indication. There is nothing to indicate that the price factor would not have been mentioned had it been of greater importance than what it appears to have been. The results, thus, indicate that the price is of subordinate importance to most housewives in their choice. However, one should take into consideration that most families have a rather stable and well established type of consumption which the price factor has already determined. If more radical changes are considered, the price factor is likely to play a more important role. As long as the consumption stays within a certain framework, the price factor seems to be of little importance even within socio-economic group III. The fact that housewives are not particularly price conscious has been confirmed by other studies.

This impression is also confirmed by the answers to other questions where the people interviewed were asked to indicate what kinds of food they would buy more or less of, if they were cheaper or more expensive, respectively. Almost everybody found it difficult to indicate what food items they would cut down on if food were more expensive. Some typical answers were:

"I don't think I can buy less of anything."

"We don't buy more than exactly what we need."

On the other hand, it was easier for people to list the food they would buy more of if it were cheaper, such as butter, meat, better kinds

of fish, vegetables, canned goods, frozen foods, coffee and various delicatessen items. Our impression from the answers to these questions is that people list groups of food which they think are expensive. However, the answers usually do not seem to be very firm or precise, which confirms the belief that the price factor constitutes only the general framework.

THE FOOD HABITS OF THE FAMILIES: GENERAL FEATURES

In order to get some idea of which family members influenced the the family's food habits the most, the persons interviewed were asked who they thought dominated the most in matters concerning food. It should be pointed out that this is no psychological description of the family but only a factual observation with regard to who actually influences the food habits regardless of the reason behind it. The reason, of course, may be factors such as a sensitive stomach or very heavy work. As table 9 shows, it is most often the husband and/or the children who have the greatest influence. The husband is only mentioned slightly more often than the children, except for socio-economic group II where he clearly is the most dominant.

A rough evaluation of the given weekly menus has been made in such a way that the number of different dishes for the main meal has been counted. Table 10 shows the division into two groups: those who only repeat one dish (that is, those who have one main meal a day prepare at least six different dishes a week; those who have two main meals a day prepare at least 12 different dishes) and those who repeat several dishes. The results show that socio-economic group I has the greatest degree of variety, socio-economic group III the lowest.

Earlier we talked about the role of the health aspects. But there was also a direct question asked: "Suppose it was discovered that fatty foods were harmful, would you then change your food habits?" Most people, 68 percent, answered yes to that question even if they sometimes had some reservations about it.

"Yes, but it is difficult; when you are used to buying rich foods you like them."

"We would have to try, if we were getting sick from the rich foods." On this point there are no significant differences between the lower groups, although the specific comments indicate that people in socio-economic group III have more reservations in their positive answers than other socio-economic groups. As shown earlier, this is also the group that uses the most fat. In a specific question it became obvious that socio-economic group III had some, although not a significant, preference for marbled or fatty pork whereas socio-economic group I preferred the lean pork. However, there are many, even in socio-economic group III, who have pointed out that they, for health reasons, have started to cut down on the fatty foods.

In order to get a picture of the families' own opinions regarding the development of their food habits, the following question was asked: "Do you think that there has been any change in your family's food habits during the last couple of years?"

Some of the typical answers were as follows:

Socio-Economic Group I:

"To leaner and healthier foods."

"It has become easier and more convenient thanks to the frozen foods."

"We have started to eat more vegetables."

"From butter to margarine, a bit more careful."

"We have made it easier; there are so many ready-made things to buy."

"Yes, we have switched from prepared desserts to fresh fruit."

"We eat more spinach."

Socio-Economic Group II:

"The dishes have become simpler."

"Food has become more expensive."

"We use more fruit and vegetables now, more canned goods and processed food."

"We have learned to like mushrooms."

Socio-Economic Group III:

"More fish now, meat is expensive."

"Food has become more expensive."

"Yes, much more fruit and vegetables; that was never used in homes of the working class before."

"People are more fussy now; what you don't like you don't eat or buy."

"Switched over to easier food, stopped serving fried potatoes, beer and such."

"One always tries something new, it is like progress."

It is obvious that many emphasize a simplification in the food habits. This means, among other things, that desserts have been simplified. A closer study of the menu shows, for instance that socio-economic group I, to a great extent uses fresh fruit for dessert, socio-economic group III to a lesser extent. People in group III still use a lot of fruit puddings, but also fresh fruit.

All the special factors which play a role in each individual case come to light in the interviewers' commentaries which are very detailed. Having a relative who owns a vegetable or fish market, or being the owner of one yourself, would naturally make a big difference, also if the family runs a children's camp. (?) In addition, it makes a difference if one or several people in the family has or has had any disease which would make it necessary to be careful of certain foods. In spite of the fact that approximately more than half the number of the families have some family member with such a disease, it doesn't seem to have much effect on the actual way of life. For the rest it can be said that the commentaries re-affirm the impression given by the previous report, that is, more vegetables in socio-economic group I, more planning and variety within this socio-economic group, etc. The influence of the children is often pointed out in the commentaries.

It should also be pointed out that on a few occasions, the interviewers commented on some very specific health aspects which the people interviewed had mentioned:

"Fp was convinced the chemical fertilizers were the reason behind 'ineffective' vegetables, which in turn cause many diseases."

"Fp thought that canned foods cause cancer; they are too clean. A few germs are good for us."

It seems as if a study of what health aspects people are actually concerned with could give some very interesting results. In this connection it should be mentioned that an estimate of calorie consumption was made.⁸ Since we lack some quantitative figures for some of the items the estimate is based only on the consumption of butter, margarine, cream, milk, cheese, eggs, bread, sugar, and potatoes. Among other things, meat, fish and vegetables are not included. The results show, however, that socio-economic group I uses 2,400 calories per consumption unit per day of the above-mentioned items; socio-economic group II uses 2,700 calories and socio-economic group III uses 3,000.

The processed foods and, especially frozen food, play an increasingly important role. It would be reasonable to assume that those who work outside the home would use these products to facilitate the cooking, but that is not the case. There is no difference in this respect between the households where the wife works outside the home and those where she stays home.

It seems as if it is not the immediate obvious circumstances, such as lack of time because of the work outside the home, which influence the greater use of these food products, but rather more individual factors, such as the housewife's wish and ability to organize her household work effectively, whether she works at home or outside the home.

The results of our study shown above have indicated, among other things, that the taste aspect is a heavily weighing factor whereas the health aspect on the other hand seems to be relatively insignificant in the consciousness of the people who were interviewed.

This indicates that changes in the food habits of the Swedish population—if such changes should prove to be medically indicated—require a different kind of intensity in the health propaganda from what it has had up till now. Judging from what we know today, the food habits seem to be better balanced in socio-economic group I than in the other socio-economic groups. This process could maybe be speeded up, especially since the noted differences in many cases do not seem to be economically motivated.

In modern society, advertising plays an important part in the direction of the effective demand. As far as food is concerned changes in demand may have both medical and production-related consequences. The more food production and food distribution become industrialized the more important the advertising will be. It is possible that the health arguments will gain importance also in Sweden. In such a case it might be appropriate to reach a consensus in time within the medical community with regard to what recommendations everybody can agree on—like a minimum: what is not harmful; like maximum: what in addition could be considered positively good for one's health. Maybe such a position would also be of interest to the agricultural policy and the investment activities of the food industry.

⁸ E. Abramsson: *Födoämnestabeller* (Lists of Foods), Stockholm, 1947, was used for the estimate.

TABLE 1.—MATERIAL OBTAINED

	Trelleborg (Tg)						Lidköping (Lk)						Total
	I		II		III		I		II		III		
	H	F	H	F	H	F	H	F	H	F	H	F	
Reported addresses	64	38	56	76	62	56	54	24	55	58	55	59	657
Unavailable—moved	3	3	1	4	3	2	4		2		2	3	27
On a diet	2		1	2	1	1			1		1	3	12
Remaining addresses	59	35	54	70	58	53	50	24	52	58	52	53	618
Sick	1		1		2	1			1			1	7
Away		1	2						1	1			5
Refused	1		1	2						2	2	1	9
Interviewed	57	34	50	68	56	52	50	24	50	55	50	51	597
Rejected		1		1		2				5		1	110
Bortsampl	7			17	6								230
Material	50	33	50	50	50	50	50	24	50	50	50	50	557

¹ Of these 10, 8 ate out in restaurants, at their parents, etc., 2 had no children at home.

² As shown, there is a varying number in the different subgroups. The reason is that the information given in the voter registry turned out to be incorrect. Since the evaluation is more simplified if every subgroup has the same number, in this case 50, a certain number were discarded at random. The number of wives working outside the home in socioeconomic group I was only 33 and 24 in Trelleborg and Lidköping, respectively, because there were no more in this group than 33 and 24.

TABLE 2.—THE CONSUMPTION OF CERTAIN FOODS PER WEEK PER FAMILY

Food and quantity	Socioeconomic group			Cities	
	I	II	III	Trelleborg	Lidköping
Butter (kg.).....	0.7	0.9	0.9	0.9	0.8
Margarine (kg.).....	.8	.7	.8	.7	.8
Cream (dl.).....	3.9	4.4	3.4	4.5	3.4
Milk (l.).....	16.0	15.6	15.5	1.5	17.9
Sugar (kg.).....	1.0	1.2	1.5	13.5	1.2
Potatoes (kg.).....	4.9	5.9	7.5	6.1	6.3
Dark bread (loaf).....	2.8	3.8	5.0	3.6	4.2
White bread (loaf):					
Trelleborg.....	2.3	2.2	2.3	2.3	1.3
Lidköping.....	1.5	1.5	1.0	-----	-----
Hardtack (¼ kg.).....	2.0	1.7	1.4	1.4	2.0
Coffee cake (loaf).....	2.3	2.5	3.2	2.2	3.2
Cheese (kg.).....	.7	.7	.7	.6	.8
Eggs (kg.).....	.8	.9	.8	.8	.9
Fruit (kg.).....	4.4	3.9	3.0	3.7	3.9

Note: The conclusion drawn in the text from the tables are based on the review of the subgroups as well as on approximate estimates of significance with the help of the so-called Arcussinus transformation on square root paper (Deming, W. E.: "Some Theory of Sampling, N.Y. 1950." The material has generally been divided according to the median. However, this will only be a rough and conservative estimate.

TABLE 3.—THE FREQUENCY OF CERTAIN FOODS OVER A 2-WEEK PERIOD

Item	Socioeconomic group			Cities	
	I	II	III	Trelleborg	Lidköping
Pork.....	2.4	2.9	3.3	3.4	2.4
Beef.....	-----	-----	-----	1.6	1.8
Trelleborg.....	2.2	1.6	1.2	-----	-----
Lidköping.....	1.7	1.8	1.8	-----	-----
Veal.....	1.2	1.2	.8	.9	1.2
Poultry.....	.7	.6	.6	.8	.4
Fresh fish.....	2.6	2.5	2.5	2.4	2.7
Frozen fish.....	1.3	.9	.6	.9	.8

TABLE 4.—MAIN MEALS ACCORDING TO THE MENU ¹

Type of main dish	Socioeconomic group			Cities	
	I	II	III	Trelleborg	Lidköping
Pork.....	2.4	2.8	3.5	3.0	2.8
Beef.....	1.2	1.2	1.2	1.1	1.4
Veal.....	.5	.5	.3	.3	.5
Total amount of pure meat.....	4.1	4.5	5.0	4.4	4.7
Ground meat.....	2.4	2.4	2.5	2.4	2.5
Sausage.....	1.5	1.7	1.8	1.5	1.8
Total number of dishes of meats and sausage.....	3.9	4.1	4.3	3.9	4.3
Organ meats.....	.7	.5	.4	.5	.6
Poultry.....	.5	.2	.2	.5	.1
Total amount of meat.....	9.2	9.3	9.9	9.3	9.7
Herring.....	.5	.7	.8	.9	.4
Other fish.....	3.2	2.9	2.4	2.3	3.3
Total amount of fish.....	3.7	3.6	3.2	3.2	3.7
Soup.....	1.9	1.3	1.2	1.3	1.5
Egg dishes.....	1.7	1.2	1.5	1.0	1.8
Vegetables as main dish.....	.3	.3	.3	.3	.3
Total number of dishes.....	16.8	15.7	16.1	15.1	17.0

¹ N equals 4,467; distributed according to socioeconomic groups and cities over a 2-week period.

TABLE 5A.—THE NUMBER OF PEOPLE WITHIN SOCIOECONOMIC GROUPS I AND II WHO USE CERTAIN VEGETABLES ONLY SEASONALLY

	Peas		Cabbage		Tomatoes		Spinach	
	I	III	I	III	I	III	I	III
Total number of users.....	154	196	133	148	147	164	127	133
Total number of seasonal users.....	6	17	15	29	110	116	16	41
Only seasonally in percent of the total number of users.....	4	12	11	20	75	71	13	31

TABLE 5B.—THE FREQUENCY OF CERTAIN VEGETABLES PER FAMILY PER WEEK

Absolute numbers	Peas			Cabbage			Spinach		
	I	II	III	I	II	III	I	II	III
Use:									
More than once per week.....	92	110	89	41	37	24	21	25	23
Once per week or less.....	60	83	107	92	133	124	106	119	110
Do not use.....	5	7	4	24	30	52	30	56	67
Total.....	157	200	200	157	200	200	157	200	200
Use (percent):									
More than once per week.....	59	55	45	26	19	12	13	13	12
Once per week or less.....	38	42	54	59	67	62	68	60	55
Do not use.....	3	4	2	15	15	26	19	28	34
Total.....	100	101	101	100	101	100	100	101	101
Tomatoes, cucumbers									
	I	II	III						
Use (percent):									
Daily.....	108	121	88						
Less often.....	39	55	76						
Do not use.....	10	22	36						
Total.....	157	200	200						

TABLE 6.—OPINIONS ON CERTAIN KINDS OF MEAT

[illegible]

TABLE 7.—OPINIONS ON FROZEN AND FRESH FISH

		Taste		Price		Variety		Tradition		Healthy		Convenience	
		I	III	I	III	I	III	I	III	I	III	I	III
<hr/>													
Frozen fish	-----	53	45	6	7	1	1	-----	8	3	76	45	
Fresh fish	-----	119	143	24	28	9	13	7	25	18	5	12	15
In percent:													
Frozen fish	-----	37	45	(4)	(7)	(1)	(1)	-----	(6)	(3)	52	45	
Fresh fish	-----	63	62	13	12	(5)	6	(4)	11	10	(2)	6	7
												I n	III n
Frozen fish	-----											144	100
Fresh fish	-----											189	229

TABLE 8.—OPINIONS ON CERTAIN VEGETABLES

		Taste		Price		Variety		Tradition		Healthy		Convenience	
		I	III	I	III	I	III	I	III	I	III	I	III
Absolute numbers													
Peas	-----	98	121	14	23	5	4	15	30	83	55	7	7
Cabbage	-----	96	93	16	20	5	8	5	14	51	34	-----	2
Tomatoes	-----	114	135	7	2	3	1	-----	2	81	62	8	13
In percent:													
Peas	-----	44	50	56	10	(2)	(2)	7	13	37	23	(3)	(3)
Cabbage	-----	55	54	9	12	(3)	(5)	(3)	8	29	20	-----	(1)
Tomatoes	-----	52	63	(3)	(1)	(1)	-----	-----	(1)	40	29	(4)	6
												I n	III n
Peas	-----											222	240
Cabbage	-----											173	171
Tomatoes	-----											219	215

TABLE 9.—THE DOMINANT FAMILY MEMBER WITH REGARD TO FOOD, DIVIDED ACCORDING TO SOCIOECONOMIC GROUPS

	Absolute numbers			Percent		
	I	II	III	I	II	III
Husband.....	37	70	47	24	35	24
Wife.....	31	31	38	20	16	19
Children.....	28	21	33	18	11	17
Husband and children.....	32	34	49	20	17	25
Other combinations or unclear.....	29	44	33	18	22	17
Total.....	157	200	200	100	101	102

TABLE 10.—DEGREE OF VARIATION IN MAIN MEALS ACCORDING TO SOCIOECONOMIC GROUPS

	Absolute numbers			Percent		
	I	II	III	I	II	III
Number of different dishes as main meal:						
6 to 7, 12 to 14.....	133	155	150	85	78	75
4 to 5, 8 to 12.....	24	45	50	15	23	25
Total.....	157	200	200	100	101	100

UNIVERSITY OF ABERDEEN,
DEPARTMENT OF CHEMICAL PATHOLOGY,
Aberdeen, AB9 2ZD, June 16, 1977.

HON. GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.*

DEAR SENATOR MCGOVERN: Thank you very much for sending me a copy of "Dietary Goals for the United States". In general I think that this is an excellent document, and have presented comments which may give additional support to some of the recommendations. My only serious reservations are in the area of dietary fat. Reduction in total calories from fat seems eminently desirable, but we do not yet understand the mechanism by which polyunsaturated fat lowers plasma cholesterol, and until this is understood it seems premature and unwise to recommend an increase in consumption of polyunsaturated fat for the total population. Furthermore, the meaning of "polyunsaturated fat" is widely misunderstood, at least in this country, so that the fat substituted may be highly undesirable (see comment, p. 616).

Equally, we do not yet understand the initiation and development of atherosclerotic plaques in human subjects. Raised plasma cholesterol is only one of several known risk factors for coronary heart disease, and it is not an obligatory factor; advanced atherosclerotic plaques are found in subjects with normal plasma cholesterol levels, and in a substantial proportion of large plaques there is no significant accumulation of cholesterol, thus cholesterol accumulation in arterial intima is not an obligatory factor for plaque development.

I fear that a campaign to increase the consumption of polyunsaturated fat may induce a sense of complacency, and thus divert efforts and funds away from serious attempts to clarify the real mechanism of plaque formation.

I apologize that the comments are much longer than I originally intended; this reflects my great interest in the problem at a whole range of different levels.

Yours sincerely,

ELSPETH B. SMITH, Ph. D.,
Senior Lecturer.

COMMENTS ON "DIETARY GOALS FOR THE UNITED STATES"
BY ELSPETH B. SMITH, PH. D.

PERSONAL QUALIFICATIONS

I should start by defining my area of competence. I am neither a nutritionist nor an epidemiologist, but since 1953 I have worked on plasma lipids and lipoproteins and their relation to coronary heart disease (CHD) and atherosclerosis in the human. Dr. Dangerfield and I published the first description of the pre- β -lipoprotein in 1955 [1],

and I defined its relationship with the VLDL ultracentrifugal fraction in 1957 [2]. My subsequent studies have been concerned mainly with the relation between plasma lipids and the lipids that accumulate in arterial wall in normal human intima with ageing, and in atherosclerotic lesions of different types and stage [reviewed in refs. 3 & 4]. Recent studies are on the quantification and characterization of plasma lipoproteins in human intima, their relation to plasma lipid levels and to retention of other plasma proteins, and factors influencing both retention and destruction of lipoprotein in intima, and the deposition of cholesterol from it [3, 4, 5, 6, 7]. In addition, I am responsible for routine plasma lipoprotein typing and screening in North-East Scotland. In collaboration with Professor Robertson of the Department of Genetics and Professor Douglas of the Department of Medicine, we are making a comprehensive study of young subject (<50 years old) with CHD, their families, spouses and spouses' families in an attempt to differentiate genetic and environmental factors both in lipoprotein level and in proneness to CHD in North-East Scotland. The study is still in progress.

COMMENTS ON TOTAL CALORIES AND SOURCES OF CALORIES (PAGES 12-29
AND 43-47.)

Scotland now has one of the highest rates of CHD in the world, high incidences of stroke, hypertension and diabetes and, in addition, there is increasing obesity, particularly amongst young people, and a serious problem with alcoholism. For the U.K. as a whole, Dorothy Hollingsworth calculated that in 1931 calorie intake equalled calorie requirement, by 1962 there was a 9 percent excess calorie intake and by 1972 an 11 percent excess intake (unpublished paper presented to Atherosclerosis Discussion Group, April, 1972). From inspection of housewives' shopping baskets it is clear that there is a very large consumption of sugar in the form of sweet cakes and biscuits, prepacked desserts, chocolate, boiled sweets and other confectionery, and soft drinks. Fresh fruit and vegetables tend to be expensive and of rather poor quality, and are not popular.

Dr. R. H. Smith, Head of the Department of Protein Biochemistry, Rowett Research Institute, Aberdeen, Scotland writes: This dietary pattern is in marked contrast to traditional pre-war diets in which brassicas (Cruciferae) cabbage, kale, Swedes and turnips figured large. Popularly, these vegetables were consumed in the form of broth (thick soup) or brose (soup with uncooked oatmeal), in which, of course, all the compounds extracted on boiling, and normally discarded with the cooking water, are conserved. The widespread popularity of brassicas (order Cruciferae), which spanned wide social strata, can be gaged by the common use of the term 'kale' (kail) to signify "broth" and thus the main meal of the day—dinner. The novelist Sir Walter Scott, for example, speaks of . . . "going home to my kail at one o'clock". Among the older inhabitants of the North-East of Scotland the kail brose is still said to be consumed regularly for the sense of well-being it brings. Fibre is an obvious dietary essential provided in good measure by these brassicas; but they also contribute an unusual sulphur-containing amino acid S-methylcystein sulfoxide (SMCO) which

may account for between 0.1 and 0.2 percent of the wet weight of the plant.

In Japan the annual production of cruciferous plants for human food is estimated at 7 M tons. This produces 12,000 tons of SMCO, providing an average of 300 mg per person per day. SMCO is thus believed to be one of the sulphur amino acids most frequently ingested from vegetable sources in Japan and this has stimulated studies of its nutritional properties. Nakamur and Ishikawa [8] and Itokawa et al. [9], have, for example, shown that in the experimental, cholesterol-fed rat, SMCO is active in lowering the cholesterol content of the plasma and liver. The possible nutritional implications of these findings are clearly evident, suggesting a possible prophylactic value against coronary heart disease for the relatively large amounts of dietary SMCO ingested in Japan.

SMCO is a relatively stable, odorless, unreactive compound and its biological activity probably arises from its conversion to dimethyl disulphide, a much more reactive (and odoriferous) compound. Thus *E. coli*, present in the alimentary tract in the rat, converts SMCO to dimethyl disulphide which, it is proposed, is associated with the cholesterol lowering reactions [10].

Support for this conjecture comes from observations with onions and garlic—vegetables belonging to another family (*Liliaceae*). The curative and prophylactic properties of these foodstuffs have been recognized from the earliest times; and more recently garlic oil has been included in the Indian Pharmacopeia, for use in cardio-vascular conditions. Garlic and onion oils are rich in alkyl polysulphides (homologues of dimethyl disulphide) which arise enzymically from S-alkyl-cystein sulfoxides, stored in the bulbs, as soon as the tissue is disrupted. Very recent publications, based on acute experiments in animals or humans, and also on human epidemiological studies, confirm that onion and garlic and their essential oils have hypolipaeamic and fibrinolysin-enhancing activities [11, 12]. Furthermore, when Augusti and Mathew [13] fed dialkyl disulphide-oxide, a constituent of garlic oil, to normal rats there was a significant fall in the lipid contents of liver and blood.

Thus the reported fall in consumption of green vegetables may have particular significance in relation to CHD ("Dietary Goals" pages 16 and 21), and the recommendation to increase consumption of green vegetables (p. 22) should be strongly endorsed.

COMMENTS ON DIETARY FAT (PAGES 30-42)

My personal observations in hospital, university and research institute canteens in Aberdeen suggest that at all levels of seniority, chips or french fried potatoes are selected with almost every main course (including salads), and that meat pies and various forms of minced beef, all of which contain large amounts of fat, are popular main dishes. In spite of the large amount of fat that accompanies the butcher's meat, housewives buy additional beef dripping and pork lard; fish is mainly fried, and served with chips. Potato crisps and savoury snacks, all with a very high fat content, are eaten between meals. Thus the chosen diet appears to have a very high fat content.

Our patients with hyperlipidaemia are advised to follow a weight-reducing diet with reduction of calories, and particularly of total fat calories, and, in a high proportion, plasma lipids return to normal in one or two months without drug treatment. Thus I believe that education of the public to reduce unnecessary fat consumption in the form of french-fried potatoes, crisps and fatty snacks, and badly prepared meat dishes, will probably reduce obesity and blood lipids, and may in the long term, influence CHD.

I do not believe that recommendations to substitute polyunsaturated fat for saturated fat are desirable, for the reasons listed below.

1. The mechanism by which polyunsaturated fats lower plasma cholesterol is not understood. Both in man and experimental animals they appear to promote a re-distribution of cholesterol from plasma into other body tissues. The findings in human studies have already been presented by Professor E. H. Ahrens, who is the world's leading authority on human sterol metabolism [14]. In experimental animals there is no decrease in total body cholesterol and consistently large increases in liver cholesterol [15, 16]. This increase in liver cholesterol is again confirmed in a very recent report (May, 1977, ref. 16); a diet high in soy bean oil increased liver cholesterol more than twofold compared with the same amount of beef tallow [16] and did not decrease serum cholesterol. Even at low levels of dietary fat, soy bean oil increased liver cholesterol by 50 percent compared with beef tallow. The authors comment "considering the 74 percent of human infants are fed high PUF milk replacement formulae [17] it is interesting to speculate that human infants may respond to a high PUF diet as do many other species".

2. It appears to me that none of the clinical trials reported so far have produced sufficiently convincing results to justify subjecting the whole population to the risk of the undesirable side effects referred to above. This area has been covered by Sir John McMichael and Professor E. H. Ahrens and I entirely agree with their conclusions. However, I would like to comment on a paper entitled "The pattern of food and mortality in Belgium" that has appeared subsequently (May 21, 1977, ref. 18), and may be quoted in support of an increase in dietary polyunsaturated fat. In North Belgium the dietary pattern has been changed to a high consumption of polyunsaturated margarine and a low consumption of butter, and the authors claim that this is associated with decreases in serum cholesterol levels, coronary morbidity and cardiovascular mortality compared with South Belgium, where there is a much higher consumption of butter. The very confused data presented are quite inadequate to support this conclusion. Comparisons of North and South are for different years, and different proportions of the populations are sampled. Death rates before the dietary change are not given, so there is no indication if change in diet has changed cardiovascular death rates in the North. Death from all causes were higher in the south, but the proportion of total deaths due to CHD was actually slightly lower in the south than in the north (24.7 percent in the south, compared with 25.25 percent in the north).

It is also of interest to look at the statistics presented in "Dietary Goals" on fat consumption (p. 35). Over the period 1909-1972, when there was a very large increase in CHD, fat consumption increased by about 25 percent, but the increase in total saturated fat was only

11 percent, and in oleic acid (mono-unsaturated) 21 percent, whereas increase in linoleic acid (polyunsaturated) was 11 percent. On p. 32 "for most years salad and cooking oils were the chief contributors" (to increased fat consumption). "However, in the last seven years meat provided the largest increase in fat". Dairy produce seems to have made an important contribution only between 1910 and 1925.

3. Teaching medical students has taught me that in Scotland the meaning of the term "polyunsaturated fat" is widely misunderstood by the public. Even third year medical students equate saturated fat with "animal fat" which they then further define as butter and cream; polyunsaturated fat is equated with "vegetable fat" and they seem to have no concept that most of the vegetable fats and oils in the supermarkets are not polyunsaturated. A good example of this public confusion is given in the table on p. 39 of "Dietary Goals" where the emotively named "non-dairy coffee whitener", which many people believe to be "safer" than cream, is shown to be 97 percent saturated, and consists of emulsified coconut oil (p. 42). Recommendations which may inadvertently lead to destruction of the dairy industry and increased consumption of stuff like this do not seem very sensible, particularly when milk is the cheapest source of protein (p. 29, table 5) and coconut oil is highly atherogenic [19]. The public would be better protected by insisting that the coffee whitener is called "emulsified, saturated fat", or completely banned.

Although corn oil, sunflower oil and safflower oil are found in health food stores, in Scotland, most of the cooking oil in supermarkets is of low price and is labelled "pure vegetable oil" or "blended vegetable oil"; I suspect that much of this is peanut oil (or rape oil, which has not yet been banned in the U.K.). Peanut oil is highly atherogenic; Wissler [19] reports: "In spite of relatively less elevation in blood lipids in monkeys fed peanut oil ration (as compared to those fed butter oil diet) the animals receiving the peanut oil consistently had the most severe lesions in their aortas". "More recently, we have extended these studies to the coronary arteries * * * with similar results." Wissler also found coconut oil to be highly atherogenic [19]. In Aberdeen I frequently find in human aortas at autopsy, large, proliferative plaques containing little lipid, which are similar to the experimental peanut oil lesions. Any dietary recommendations that could inadvertently lead to increased consumption of peanut oil, seem highly undesirable.

4. When I started working on human arterial wall, I took it for granted that plasma lipids and lipoproteins were the primary factors in atherogenesis: now I am increasingly impressed by the complexity of the molecular interactions that they occur between several plasma proteins and the extracellular matrix of the arterial wall, and between the plasma proteins themselves within the wall. Thus all plasma proteins appear to be present in adult human intima, and their concentrations are increased in early fibrous plaques. In these precursor lesions, accumulation of the blood clotting protein, fibrinogen, is increased to an even greater extent than accumulation of lipoprotein. As the plaques develop, soluble fibrinogen appears to be converted to insoluble fibrin, which may in turn play some role in "binding" lipoprotein [6, 20]. In many early fibrous (gelatinous) plaques the concentration of cholesterol is no higher than in adjacent normal intima, and may

even be lower. Thus accumulation of cholesterol in intima is not an obligatory factor for development of atherosclerotic lesions [21]. Equally, raised serum cholesterol is not an obligatory factor for development of clinical CHD; about one third of patients with CHD have raised plasma lipids, but in two thirds of patients the plasma lipids are within the normal range (see, for example 22 & 23). In one study serum cholesterol was below 200 mg. percent in 28 percent of patients [23]. Even in the younger patients with CHD in our present study, two thirds have plasma lipid levels within the normal range.

I fear that a campaign to increase consumption of polyunsaturated fat may, inadvertently, increase consumption of the wrong types of vegetable fat, may fail to reduce the incidence of CHD, may produce undesirable side effects, and will certainly divert finance and effort away from fundamental research on the mechanisms involved in atherogenesis.

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BEVERLY HILLS, CALIF., July 1, 1977.

HON. GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs, U.S.
Senate, Washington, D.C.*

DEAR SENATOR: Enclosed are my recommendations and thoughts in general on Dietary Goals for the United States, as requested by you in your letter of May 16.

With best wishes.

Sincerely,

ELIOT CORDAY, M.D.

Enclosure.

REPORT TO SELECT COMMITTEE ON NUTRITION AND HUMAN NEEDS
DIETARY GOALS FOR THE U.S.A.

I have studied the "Dietary Goals for the United States" prepared by the staff of the Select Committee on Nutrition and Human Needs for the U.S. Senate. However, in my humble opinion I advise that it is premature to begin to apply these goals, because the diet has not yet been tested to determine whether it is effective in reducing obstructive arteriosclerotic disease of the heart, brain and other organs, or even whether it might cause a certain detriment to the health of the nation. I recommend that the time is not yet ripe for changes, and we must wait until simple hard facts are obtained on possible benefits of a prudent diet utilized in N.I.H. population studies entailing the multiple risk factor intervention trials, the lipid research clinics and follow-up programs are completed within the next two to five years. I note that the new U.S. dietary goals prepared by the staff of the Senate Select Committee on Nutrition and Human Needs are principally based upon the assumption that arteriosclerosis, our nation's greatest killer, obstructs the arteries by a lipid infiltration from the blood into the arteries, and that reduction of fats in the diet will reverse or prevent that fatal process. Therefore, it is assumed that reshaping the eating habits of some 215 million Americans will prevent the occurrence of obstructive lesions and restore or maintain the nation's health. Lipid disorders can be detected in the blood of an afflicted individual. It would appear to be a causative factor in only 5 to 20 percent of the American public. It seems unwise to tamper with the diets of the great majority of the U.S. population until we have more knowledge about whether dietary modifications in the clinical trials can prevent arteriosclerosis in man. The new dietary goals might, in fact, be detrimental as it has been demonstrated by scientific study that a fat-free diet for the infant or child can result in abnormal development of the brain and nervous system. It would seem more advisable to apply low fat diets to a limited number of clinically discernible individuals identified by simple clinical tests rather than to the masses who depend upon such foods as milk for their principal food source.

I utter these words of caution as a clinician, research scientist, not a nutritionist. But I believe I am capable of interpreting the effects

of diet because of my 37 years in research investigation and clinical practice. I served as a member of the National Advisory Council of the National Heart, Lung and Blood Institute in the years 1969 to 1974, on the Joint Council Subcommittee on Cerebrovascular Disease from 1969 to the present, as a member of the Advisory Panel on Heart Disease to the President of the United States in 1972, as National Consultant in Cardiology to the Surgeon General of the U.S. Air Force from 1967 to the present. I am a Clinical Professor of Medicine at UCLA and Chairman of the Cardiac Care Committee of the Cedars-Sinai Medical Center. I have published over 300 research studies on heart and cerebrovascular disease, and am the author of five textbooks. Through my years of service in various branches of the N.I.H. and the President's panel, I have recognized that arteriosclerosis continues to be our greatest killer, and that it injures, disables, and causes suffering to several million individuals in our country each year. In our editorial on "Prevention of Heart Disease by Control of Risk Factors: The Time Has Come to Face the Facts," published in February 1975, we stated that through the years we have become aware that segments of research information have often been pulled together prematurely and the population propagandized into believing that the problem of arteriosclerosis has been conquered.

The monumental work of the Framingham Study elucidated some of the precursors of coronary and cerebrovascular disease some 27 years ago. It indicated that elevated levels of serum lipids including cholesterol phospholipids, beta and prebeta lipoproteins, hypertension, obesity, low vital capacity, electrocardiographic abnormalities, diabetes, genetic disposition, smoking, and sedentary life were all associated with increased incidence of coronary disease. The Heart and Lung Institute appointed a Task Force on Arteriosclerosis who re-evaluated the currently available information on arteriosclerosis and formulated recommendations for long range programs in their report in 1971. In the year long deliberations by a Blue Ribbon Task Force of 102 scientists, they cast doubt on many beliefs now accepted as gospel and formulated recommendations on long range programs. The report implied that we do not understand the basic mechanisms underlying development of the arteriosclerotic lesions, nor how various risk factors bring about the development of clinical disease. It indicated that the major means of preventing and treating heart disease have yet to be elucidated. It also indicated that we must question whether reduction of the risk factors will (1) stop progression of arteriosclerotic lesions in the majority of patients, or (2) reverse the lesions once they become manifest. The Report also stated there is no conclusive evidence that preventive measures based on correction of a single risk factor will prevent arteriosclerotic heart disease. However, it hypothesized that if interventions to reduce multiple risk factors such as hypertension, cholesterol levels and smoking habits were applied in combination that it might retard the obstructive process. The Task Force has since recommended a test of this hypothesis. The Multiple Risk Factor Trial (MR FIT) was initiated in the year 1972. During the Fiscal Years 1972 to 1976 this population study has been funded for over \$52,750,854. When the MR FIT program is completed by the year 1982, it will determine whether a comprehensive preventative program directed at reduction of a combination of these three risk

factors will significantly reduce the incidence of myocardial infarction deaths from coronary disease.

If this monumental study fails to demonstrate that control of diet and the two other risk factors, I see little hope that alterations in the U.S. diet as recommended by the Select Committee on Nutrition and Human Needs could be effective in prevention of arteriosclerotic disease. There have been repeated utterances from the medical profession that possibly too much emphasis has been placed on lipids as a cause of arteriosclerosis, that there is as yet no confirmed efficacy of lowering the lipids. Possibly the Select Committee on Nutrition and Human Needs should consider a population study to be performed to test the effectiveness of the dietary goals as laid out by this study to determine whether it will (1) reverse the established lesion, and (2) whether it will prevent the progress of the disease process. The dollar cost of performing such population studies as a possible form of preventative medicine is rather high. However, the ultimate cost of arteriosclerosis, the nation's biggest killer accounting for one million of the 1,800,000 deaths each year in the United States, costs many billions in cost of medical care and loss of payroll taxes. The total health care expenditures in the fiscal year 1980 is projected to be \$230 billion. Therefore, before a change of dietary goals is applied to the nation to prevent arteriosclerosis, it behooves the health planners to test the hypothesis of alterations in nutritional risks with the diets advocated by their health advisors. The costs of such studies are infinitesimal compared to costs of health care, loss of productivity, and creativity, and the humanitarian goal of preventing vast suffering. However, I would ask that the Senate Committee to realize that the "Dietary Goals for the United States," page five, published the statement—

dietary trials might not provide any effectiveness because once hypertension, diabetes, and arteriosclerotic disease are manifest, there is in reality very little medical science can do to return the patient to normal physiological function.

I further recommend that the Senate Committee obtain the opinion of the renowned specialists who are serving on the food and nutrition board of the National Academy of Sciences on the possible benefits and detrimental effects of the recommended dietary goals. I must caution the committee that the alterations in diet could cause malnutrition, and also that because of the high cost of carbohydrates and prohibitive costs of fruits except in a short peak season, the majority of the population would not be able to afford such foodstuffs. They would not be able to purchase foods of sufficient nutritive value and might suffer the effects of malnutrition. A study should first be performed to see whether it is advisable to reduce the butterfat content by substituting non-fat milk for whole milk. It has been well demonstrated that in the casualties of the Vietnam-Korean wars that the first signs of arteriosclerosis may begin just about the time of birth, and that it incubates slowly through a latent period until it produces clinical manifestations of obstructive disease in middle age. Therefore, if methods are to be effective they should be applied starting in the pediatric age group. Of course, it will take some 50 years to determine whether such interventions are effective in preventing obstructive lesions that can be detected clinically. The real question remains

whether a cholesterolgenic diet is harmful to all Americans or to a limited number of clinically discernable individuals.

We must also realize that less than 20 percent of patients admitted to coronary care units or to a surgical service for repair of obstructive vascular lesions have an abnormal lipid pattern. We therefore must question whether application of an unproven diet blanketed to the population as a whole would be advisable. This seems to me like asking the whole nation to wear a size 12 patent leather shoe. Because familial hypercholesterolemia is associated with premature arteriosclerosis and can be detected by blood analysis, it would be better to identify the few individuals at risk by such diagnostic screening tests and ferret out the susceptible individual for measures prescribed by the proposed dietary goals.

The recommendations of the Select Committee on Nutrition and Human Needs strongly implies that following Congressional adoption of suggested dietary guidelines will result in a lowered incidence of coronary disease. It has not been clearly shown that lipid lowering, dietary or drug regimen reduces the incidence of coronary disease, and, secondly, it has not been proven that the lowering of lipids will reverse the arteriosclerotic lesion. Is it possible that the advisors of dietary goals are barking up the wrong tree? Moderate changes in the proposed dietary goals can't be expected to lower the levels of plasma lipids far enough to have a desirable effect on coronary disease incidence. New investigations indicate that the lipid hypothesis has not yet been proven to be completely correct, and that not enough information has been available about nutrition in relation to coronary and cerebral vascular disease to be able to advise the public and the practitioners of an acceptable program.

In conclusion.—I would like to plead that the recommendations of the Select Committee on Nutrition and Human Needs be deferred until further study will determine whether proposed dietary change can actually prevent arteriosclerosis or reverse the obstructive process, and also determine whether the population can afford the cost of such dietary changes under the present marketing system. I seriously question from a public health standpoint whether alterations in nutritional risk factors will lead to significant reduction in death or disability from coronary disease. Unless the medical profession and nutritionists are convinced by proven clinical evidence of the benefits of a new dietary goal, that it is a safe and cost-effective, efficient way of preventing coronary disease or cerebrovascular disease, we can assume they will not apply the recommendations to their clinical practice. Present FDA edicts demand proof that a single pharmaceutical agent is safe as well as beneficial. Can we except the practitioner to demand that their patients accept the dietary goals without proof of safety or clinical benefits?

If present mass population studies do not prove to be effective in preventing arteriosclerosis, the hope for coping with our principal health problems will place us in a state of bankruptcy in a public health sense. We must realize that further research investigation must take place upon prospective avenues that might provide better prevention of familial hyperlipidemias where all the males die in a family before

they reach 40 years of age, and the females die some 10 years later after their menopause, suggesting some hormonal factor is to blame. This suggests the health agencies might initiate future endocrine research that could lead to a more practical solution. Furthermore, we must realize that a form of galloping atherosclerosis occurs in individuals with immunologic problems such as in the transplanted heart, or lupus erythematosus. Transplant patients and those suffering from diabetes melitus could provide accelerated models for testing preventative measures against atherosclerosis. Imaginative investigators might well look for other likely causes which, when identified, could be investigated thoroughly by a disciplined program managed by the scientists who were brought together in specialized national centers. If such programs could be fashioned and financed with the same sense of urgency with which our nation dramatically pursued the atomic energy missile and space program, arteriosclerosis might be conquered. The knowledge in the basic mechanisms underlying arteriosclerosis and how risk factors might influence the progress of the lesion are seriously lacking. Until the gaps in knowledge are filled in, it will be difficult to provide a rational program of prevention and treatment. We must encourage our Congressional leaders to realize that if the multiple risk factor trials fail to prevent progress of arteriosclerosis, we really have no promising public health measures. In planning the defense of a country, the military plan for all future eventualities includes possible failure. In my humble opinion, the scientific community, our Congressional leaders, and the N.I.H. should have plans under way in case the multiple risk factor trials fail to provide a defense against our nation's biggest killer. Our Congress must provide the highest priority of funding to encourage a more massive research program on arteriosclerosis.

UNIVERSITY OF MARYLAND HOSPITAL,
Baltimore, Md., August 15, 1977

SELECT COMMITTEE ON NUTRITION AND HUMAN NEEDS,
U.S. Senate,
Washington, D.C.

DEAR COMMITTEE MEMBERS: After having had an opportunity to read the goals of the Senate Select Committee on Nutrition and Human Needs and read some of the rebuttal, I would like to write my opinion.

I believe the goals and the methods of implementation are quite commendable and strongly support them, although the factual basis upon which these goals are worked out is not now, nor never will be, entirely precisely known to everyone's satisfaction. The measures proposed would in everybody's agreement be those directed toward benefit with a very limited possibility for harm. I believe goals will change as new information appears, but that these directions and reeducation away from a meat and dairy product poultry concept, along the lines presented, are healthy ones and am supportive.

Sincerely,

FRANK L. IBER, M.D.
Professor of Medicine,
University of Maryland, School of Medicine.

GENERAL CONFERENCE OF SEVENTH-DAY ADVENTISTS,
Washington, D.C., August 15, 1977.

*Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.*

We have read with much interest the report of the Senate Select Committee on the Dietary Goals for the USA. The principles are sound and have been tested for many years. The Seventh-day Adventist church for more than 100 years has been advocating the importance of dietary practices to health and longevity.

Examples may be seen in the Hunza people of Asia and other groups beside Seventh-day Adventists, of the value of fruits, grains, nuts and vegetables to our general health.

We recommend these benefits to the American people at large as a means of lessening mortality and morbidity rates, and of enjoying better health and productivity. Enclosed are materials to further explain and support our position.

We commend our government for these bold moves to bring to the public these suggested goals, and further, we pledge our support in this action.

Sincerely,

S. L. DeSHAY, MD, MPH,

Director.

ELLA MAY STONEBURNER, RN, MS,

Associate Director.

Enclosures.

[From Journal of The American Dietetic Association, Vo. 62, No. 3, March 1973]

SCIENTIFIC AND PRACTICAL CONSIDERATIONS—THE VEGETARIAN
DIET¹

(By U. D. Register, Ph. D., R.D., and L. M. Sonnenberg, R.D., Department of Nutrition, School of Health, Loma Linda University, Loma Linda, Calif.)

Large populations of the world have lived for centuries on diets considered near-vegetarian because of economic necessity and availability of little or no animal products. Today, however, in an affluent society where food supplies are abundant, an interesting trend has been developing in that more and more Americans, particularly young adults, are becoming vegetarians.

There are a number of reasons which vary as to the type of diet adopted, adherence to it, and other characteristics of life style. A common objective appears to be that of promoting health and a sense of well-being although many individuals turn to vegetarian diets for their own personal reasons without adequate information of food values and nutritional principles. The use of Zen macrobiotic diets is a well known example of problems that potentially may develop when the diet is improperly selected.

¹ Presented at the 55th Annual Meeting of The American Dietetic Association in New Orleans, on Oct. 11, 1972.

The Zen macrobiotic regimen basically consists of ten diets, ranging from the lowest level (diet 3) which includes fruits, vegetables, and some animal products in addition to cereals, to the highest level (diet 7) made up entirely of cereals. Individuals who persist in following the more rigid diets are in great danger of developing serious nutritional deficiencies. Cases of scurvy, anemia, hypoproteinemia, hypocalcemia, emaciation due to starvation, and other forms of malnutrition, in addition to loss of kidney function due to restricted fluid intake, have been reported, some of which have resulted in death [1].

There is a vast difference between people who are vegetarians by choice and those who have no other alternative because of economics and available food supplies. Both groups can benefit from the assurance that their diets can be adequate and healthful. To understand and to be prepared to provide professional counsel and assistance are challenges to all involved in nutritional care.

PROTEIN IN THE VEGETARIAN DIET

Quantitative aspects.—German physiologists recommended high protein intakes based on their opinion that protein need was proportionate to muscular activity [2]. Voit based his recommendation for an intake of 120 gm. protein on his survey among German workers who were eating a high-protein diet. [3]. However, controlled experiments using the nitrogen balance method showed that normal subjects can maintain nitrogen equilibrium on protein intakes of from 30 to 35 gm. per day [4].

In 1946, Hegsted et al. studied adults on an all-plant diet in which cereals provided 62 per cent of the protein. They concluded [5] that on this type of diet, 30 to 40 gm. protein per day would meet minimal requirements of a man weighing 70 kg.

A comprehensive nutritional study by Hardinge and Stare [6] in 1954 compared nutritive intake and nutritional, physical, and laboratory findings of 200 subjects on three types of diets: twenty-six pure vegetarians, who used no animal products; eighty-six lacto-ovo-vegetarians, who used milk and eggs; and eighty-eight non-vegetarians. No evidence of deficiency was found, and each group met or surpassed the Recommended Dietary Allowances. These results showed that the average protein intake of the adult men on the pure vegetarian diet was 83 gm.; on the lacto-ovo-vegetarian diet, 98 gm.; and on the non-vegetarian, 125 gm. Results for women were 61, 82, and 94 gm., respectively. Dietitians accustomed to computing meatless menus find it difficult not to exceed the protein allowances when caloric needs are met.

Hegsted and the Harvard group have commented [7] that for adults "it is difficult to obtain a mixed vegetable diet which will produce an appreciable loss of body protein without resorting to high levels of sugar, jams, and jellies, and other essentially protein-free foods." Similar experiences have been found in our laboratories.

Total serum protein, albumin, and globulin values and the hematologic findings for the vegetarian and non-vegetarian groups in Harding and Stare's study were not statistically different. The pure vegetarians averaged 20 lb. less in weight than the others who averaged 12 to 15 lb. above their ideal weight.

Although protein has been singled out for attention in populations where malnutrition is prevalent, the problem is often compounded by a total caloric deficit. Even when an adequate amount of protein is provided, symptoms of protein deficiency may still appear if the diet does not also provide sufficient calories since, under these circumstances, some of the protein is utilized for energy.

In a review of cereal diets in which 10 per cent or less of the protein calories were derived from animal sources. Ohlson reported [8] that the adult protein requirements, as analyzed by FAO, probably could be met if sufficient calories were available. She found that 2,500 kcal from such a food mixture would, on the average, supply 67 gm. protein—almost 50 per cent more protein than estimated to be adequate for 98 per cent of the adult population.

In India, the average caloric intake is about 2,050 kcal per day, supplying a total of 57 gm. protein, of which 51 gm. come from plant sources [9]. By contrast, in the United States, the average intake is approximately 3,200 kcal with a total of 97 gm. protein, of which 31 gm. is from plant sources. By increasing the Indian diet 1,000 kcal (comparable to the caloric level in American diets), there would be an increase of 25 gm. plant protein. With this caloric increase, the total protein level in the Indian diet would be 82 gm., considerably exceeding recommendations.

In a review of current concepts of protein nutrition, Scrimshaw of Massachusetts Institute of Technology asks [10]: "How do we allow adequately for individual variation without recommending a wasteful margin of safety?" To answer this question, at least for young adults, he studied 100 young men, all university students, who were given a diet adequate in calories but lacking in protein. His studies indicated that generally an amount less than 30 gm. protein daily is adequate for normal activities. Nitrogen balance at these low levels of intake was possible only because a protein of excellent quality, that of freeze-dried whole egg, was used. A correction for the lesser protein quality of ordinary mixed diets must be made. Scrimshaw makes the point that absolute requirements for protein in healthy adults are much lower than commonly suggested, provided the quality is good.

Scientific studies continue to confirm Sherman's findings [11] that 1 gm. protein per kilogram body weight provides a liberal margin of safety for adult maintenance. This is reflected in the 1968 revision of the Recommended Dietary Allowances, which are practical and desirable levels. The importance of planning adequate diets to meet these allowances has been amply substantiated, not only by research but by clinical studies and human experience. Table 1 shows how easily protein needs can be met on a lacto-ovo-vegetarian diet. It will be noted that the protein total for two meals is about 60 gm., approximately twice the minimum requirement for adult man.

TABLE 1.—2 menus to meet protein needs from typical lacto-ovo-vegetarian meal patterns¹

Food	Protein (gm.)
Menu I:	
Oatmeal and raisins.....	4
Milk, 1 glass.....	8.5
Bread, 2 slices whole wheat toast.....	5
Fruit, 1 serving.....	1
Egg or meat analog (1-2 oz.) or nuts (½ oz.), or peanut butter (1 Tbsp.)	5-6
Total	24
Menu II:	
Lettuce and tomato salad.....	2
with cottage cheese.....	15
Entrée	12
Peas	5
Potato	3
Bread, whole wheat.....	2.5
Milk, 1 glass.....	8.5
Dessert	3
Total	36

¹ Total for 2 meals equals approximately 60 gm. protein; values for the 3rd meal are not included.

Qualitative aspects.—The extensive fund of knowledge supplying information in regard to the amino acid composition of foods has been achieved through a number of methods of experimentation. Among these are animal growth studies, biologic value methods, nitrogen balance studies, and dietary surveys, as well as chemical and chromatographic determinations.

A number of the very early studies used the rat growth method for evaluating the quality of single proteins. By this method, the quality of plant proteins was generally undervalued. However, the concept of mutual supplementation evolved. As pointed out in *The Lancet* [12]: "Formerly vegetable proteins were classified as second-class and regarded as inferior to first-class proteins of animal origin; but this distribution has now been generally discarded. Certainly some vegetable proteins, if fed as the sole source of protein, are of relatively low value for promoting growth; but many field trials have shown that the proteins provided by suitable mixtures of vegetable origin enable children to grow as well as children provided with milk and other animal proteins."

Bressani and Behar have stated [13]: "From a nutritional point of view, animal or vegetable proteins should not be differentiated. It is known today that the relative concentration of the amino acids, particularly of the essential ones, is the most important factor determining the biological value of a protein. * * * By combining different proteins in appropriate ways, vegetable proteins cannot be distinguished nutritionally from those of animal origin. The amino acids and not the proteins should be considered as the nutritional units."

Since wheat is so widely used, early studies [14] of the supplementary value of wheat protein with other proteins were carried out in this laboratory. Because wheat is low in lysine, foods that are relatively high in this amino acid were tested. We found that when 70 percent of the protein in the diet was from wheat protein and the remaining 30

percent from milk, yeast, nuts, soybeans, and other legumes, excellent supplementary action occurred as judged by rat growth.

In a study by Sanchez, Porter, and Register [15], a week's hospital vegetarian diet containing milk and eggs was fed to a group of animals, and their growth was compared with that of a group of animals receiving the same diet in which meat replaced the plant protein entrées. The results showed no significant difference. The average growth of the animals on the meat and meatless diets was 39 and 37 gm. per week, respectively.

Sanchez et al. designed a study [16] to evaluate by the biologic value method the protein content of complete meals. All basal meal patterns consisted of portions from plant foods and were tested together with supplements of lysine, soybean milk, cow's milk, or a combination of these supplements. When diets were formulated to contain grain-legume mixtures as eaten in most countries, biologic values were above 70 and compared favorably with diets containing meat, milk, and lysine. These results suggest the possible supplementary value of proteins in diets of peoples of many countries which include large quantities of cereals, some legumes and possibly some other vegetables, fruits and nuts, and little or no animal foods.

Using the nitrogen balance method, Register et al. evaluated [17] in human subjects the protein quality of diets containing vegetable protein mixtures prepared to simulate meat products. The results were compared with similar diets containing milk and beef. Six university students served as subjects in each of four tests. At an approximately 60-gm. protein level, selected diets containing prepared vegetable protein mixtures with soybean milk or cow's milk maintained nitrogen balance. Such diets also compared favorably with the non-vegetarian diet in maintaining nitrogen balance.

The metabolic response of eighteen-year-old adolescent girls to a lacto-ovo-vegetarian diet was studied by Marsh and co-workers [18]. The calculated essential amino acid intake was far in excess of the minimal requirement for women for every amino acid.

Edwards et al. did nitrogen balance studies on twelve men at the beginning and end of four, fifteen-day intervals following the ingestion of wheat diets containing 46 gm. protein per day. They found [19] that nitrogen balance was maintained over a period of sixty days.

In studying vegetarians, Hardinge, Crooks, and Stare analyzed [20] the essential amino acids of the dietary proteins of the subjects. Their figures showed that the intake of all groups ranged from more than twice to many times the minimum essential amino acid requirements (table 2).

Evaluating protein quality by various methods has resulted in a large body of information that provides scientific basis for planning vegetarian diets that are quantitatively and qualitatively adequate. Understanding of protein nutrition has progressed to the point where an all vegetable combination, such as Incaparina, is completely adequate in feeding very young children, even those suffering from malnutrition.

In the developing countries, this concept of mutual amino acid supplementation has sparked investigations into many single plant sources to determine combinations of available supplies which supplement each other. Rao and Swaminathan summarized [21] a number of these

studies: peanut proteins supplement wheat, oat, corn, rice, and coconut proteins to a significant extent; being rich in lysine and valine, soybean proteins supplement those of wheat, corn, and rye; a mixture of soy and sesame proteins has a high nutritive value comparable to milk proteins; and the proteins of legumes and leafy vegetables remarkably supplement those of cereals.

TABLE 2.—ESSENTIAL AMINO ACIDS IN DIETS OF ADULT MALE VEGETARIANS AND NONVEGETARIANS¹

Amino acid (grams)	Non-vegetarian	Lacto-ovo-vegetarian	Pure vegetarian	Recommendation ²
Isoleucine.....	6.6	5.4	4.0	1.4
Leucine.....	10.1	8.2	6.0	2.2
Lysine.....	8.3	5.4	3.7	1.6
Phenylalanine plus tyrosine.....	10.4	8.8	7.0	2.2
Methionine plus cystine.....	4.3	3.2	2.7	2.2
Threonine.....	5.0	3.8	2.9	1.0
Tryptophan.....	1.5	1.2	1.1	1.5
Valine.....	7.1	5.6	4.3	1.6
Protein intake.....	121.3	97.2	81.5	65.0

¹ Taken from Hardinge, Crooks, & Stare (20).

² Recommendation is twice the minimum requirements.

In a paper on current concepts of protein nutrition, Scrimshaw declares [10]: "Vegetable mixtures supplying the amino acids in appropriate proportions are as efficient in meeting protein needs at minimum levels of intake as proteins of animal origin." Recent advances in our understanding of protein requirements, he says, free us "from dependence on the concept of the need for animal protein or amino acids from conventional food alone and allows us to concentrate on ways of most efficiently and economically meeting man's need." He further states that the "bulk of present and future needs will be met by conventional plant proteins."

Information from studies on the supplementary relationship of plant proteins has resulted in the development and marketing of a number of formulated plant protein foods referred to as "meat analogs." A number of these products combine various proportions of legumes, nuts, and cereals. One advantage of all of these foods is that, since they are made of plant sources, they do not contain cholesterol or saturated animal fats.

Soy products

Vegetable proteins that are finding special consumer interest are the spun soy and textured soy protein products. They offer great potential and versatility because they can be formulated to any protein, fat, or carbohydrate level desired, and proteins may be blended to accomplish a very favorable amino acid composition.

Since spun soy isolates are the purified protein fraction of soybeans, it is important that they be fortified or used in combination with foods which contain the essential nutrients, such as iron and a number of the B vitamins which meat proteins provide in the diet. The U.S. Department of Agriculture's Agricultural Research Service has set up compositional requirements for textured vegetable protein products for use in the school lunch program [22].

Based on casein as a standard with a protein efficiency ratio (PER) of 2.50, ham analog has a PER of 3.10; smoked turkey analog, 2.81; plant protein wieners, 2.50; textured protein sausage, 2.40; and chicken

analog, 2.34. Meat analogs also usually contain less fat than their meat counterparts. Ham analog has only 12 percent fat compared with about 30 to 35 percent for ham; plant protein wieners, 12 percent compared with up to 30 percent for meat wieners; and beef analog, 12 percent compared with 18 to 23 percent for beef [23].

TABLE 3.—EXAMPLES OF ADEQUATE AND INADEQUATE NEAR NONFLESH AND NONFLESH DIETS OF POPULATION GROUPS REPORTED IN THE LITERATURE¹

Investigator	Population group	Characteristics of the diet
Adequate diets:		
McCarrison	Hunza	Wheat, barley, millet, maize, legumes, vegetables, apricots, milk, meat occasionally.
Richards	Bemba	Finger millet, maize, sweet potatoes, legumes, plantains, vegetables, little animal food.
Steiner	Okinawans	Rice, sweet potatoes, soybeans, vegetables, some milk, meat infrequently.
Adolph	North Chinese	Wheat, millet, barley, corn, soybeans, other legumes, vegetables.
Anderson et al.	Otomi Indians, Mexico	Corn (mainly as tortillas, up to 80 percent of total calories), legumes, vegetables, fruit, animal protein low.
Toor et al.	Yemenite Jews	Large quantities of "pita" (flat bread) and vegetables, sunflower seeds, legumes, nuts, little meat.
Walker	South African Bantu	50 to 90 percent whole-ground or lightly milled cereals, corn, sorghum, and wheat, legumes, vegetables and greens; a little milk, eggs, and meat.
FAO/WHO Report	Lebanese	56 percent of calories from cereals—wheat, barley, millet, rice; milk, cheese, legumes, fruits, vegetables, olive oil, and ghee; meat intake very low.
Inadequate diets:		
McCarrison	India, poor southern	Mostly white rice, some legumes, vegetables, fruits, little or no milk or meat.
Gillman	Poor Bantu	Diet largely maize meal (mealie pap) and sour milk when available.
Oomen et al.	Papua, Highland	Sago, sweet potato, or taro, often providing 90 percent of total calories.
Bailey	Java (cassava area);	Poor man's diet; cassava root providing 95 percent of calories, vegetables 4 percent, and beans 1 percent; total calories, 1,600; total protein, 9 gm.
Collis et al.	Nigeria (Yoruba)	Starchy roots and starchy portion of grains, fruit rarely eaten, low intake of pulses and animal products.
Orr and Gilks	Africa (Kikuyu)	White millet, maize, some legumes and vegetables, a little milk, but taboo for women from puberty to menopause.
De Wijn	Central Celebes	Rice providing 82 percent of calories, coconut 11 percent, vegetables 1 percent, a little fish and coconut oil.

¹ From Hardinge & Stare (27).

In a study by Koury and Hodges [24], prison volunteers were hospitalized and placed on a diet for twenty-four weeks with soy protein foods as the only source of protein. The diet was well accepted, weight was maintained, and all subjects remained in good health. Laboratory results showed normal findings for hemoglobin, hematocrit, and urea nitrogen, indicating that the protein was well utilized. Serum cholesterol and triglyceride values were markedly influenced by the diets. The average decrease in serum cholesterol was approximately 100 mg. per milliliter.

Bressani et al. compared the protein quality of textured soy protein with meat and milk in experimental animals and children [25]. Growth was the same for dogs fed soy protein as for those fed meat. Even when large amounts of soy protein were given, no adverse physiologic effects were observed. Nitrogen absorption and retention were essentially the same for both the milk and soy protein diets of children. It was concluded that the protein quality of soy protein is high, about 80 percent of the protein quality of milk, with adequate digestibility.

As the world protein supply dwindles in relation to the population growth, textured protein products will be used to supplement and extend existing protein sources. A recent Cornell University study [26]

forecasts that meat analogs and extenders may reach 10 percent of all domestic meat consumption by 1985, certainly by year 2000. This would represent an increase from the present level of 145 million lb. per year to approximately 2.45 billion lb. in 15 years.

Adequate and inadequate vegetarian diets

Worldwide studies of properly selected vegetarian diets support the adequacy of such a dietary pattern. True, many reports have been published of nutritional diseases prevalent in underprivileged areas of the world. These generally show that the diseases are due, not to a vegetarian diet as such, but to a gross shortage of food, or to a diet consisting largely of such foods as refined cornmeal, cassava root, tapioca, or white rice, with practically no milk, eggs, leafy vegetables, legumes, or fruits. Lack of suitable post-weaning foods affect young children, particularly. Parasitic infestations frequently accentuate the symptoms of nutritional diseases in these areas.

Hardinge and Crooks reviewed the scientific literature on vegetarian and near-vegetarian diets [27]. Tables 3 and 4 summarize their findings. They conclude that "widely differing dietary practices appear among vegetarians and near-vegetarians. A reasonably chosen plant diet, supplemented with a fair amount of dairy products, with or without eggs, is apparently adequate for every nutritional requirement of all age groups.

"Pure vegetarian diets, the use of which produced no detectable deficiency signs, contained adequate calories obtained mainly from unrefined grains; legumes; nuts and nut-like seeds; a variety of vegetables, including the leafy kinds; and usually an abundance of fruits.

"Vegetarian and near-vegetarian diets that have proved inadequate include: (a) vegan diets which have been reported to produce vitamin B₁₂ deficiency in some individuals; (b) grossly unbalanced near-vegetarian diets in which as much as 95 percent of the calories were provided by starchy foods extremely low in protein, such as cassava root; (c) diets dependent too largely on refined cereals, such as cornmeal or white rice, even though small amounts of animal foods were included; and (d) intake of total calories insufficient for maintenance requirements."

Plant dietaries and serum lipids

Experimental studies and epidemiologic findings on the lipid-lowering effect of plant dietaries may have great significance for current problems in nutrition and public health. The pure vegetarians in a study by Hardinge and Stare [28] had significantly lower serum cholesterol than either the lacto-ovo-vegetarians or non-vegetarians.

Serum cholesterol and the dietary habits of a voluntary group of 466 Seventh-Day Adventists (sDA) were studied to determine the influence of diet on serum cholesterol in an adult population whose main environmental differences related to their adherence to a vegetarian diet. West and Hayes matched vegetarians with non-vegetarians from the same base population and examined the effects of various levels of meat, fish, and fowl consumption (degrees of non-vegetarianism) on serum cholesterol levels [29]. The difference between serum cholesterol of the vegetarians and non-vegetarians was statistically significant. Several degrees of non-vegetarianism were noted, and the evidence was

clear that as the degree of non-vegetarianism increased, the serum cholesterol increased.

Lemon and Walden, in their study of California Adventists, showed [30] that male SDAs suffered their first heart attack a full decade later than most Americans, and the incidence of heart disease was only 60 percent of the average California male population. Hodges et al. fed a diet to men in which the source of protein was meat analogs; they reported [31] a significant decrease in serum cholesterol.

TABLE 4.—GREENS COMPARED WITH MILK AS SOURCES OF NUTRIENTS

Food ¹	Protein (gm)	Calcium (mg)	Riboflavin (mg)	Iron (mg)	Vitamin B ₁₂ (mcg)
Milk.....	7.0	234	340	0.2	1.2
Soy milk ²	6.0	60	120	1.5	.6
Broccoli.....	7.2	206	460	2.2	-----
Turnip greens.....	6.0	490	480	3.6	-----
Greens, average ³	6.7	305	390	3.0	-----
Soybeans, green.....	19.6	120	260	5.0	-----

¹ 1 cup or 200 gm.

² Commercial.

³ Greens included: broccoli, brussels sprouts, collards, dandelion greens, kale, mustard greens, spinach, and turnip greens.

Although the type and amount of fat, as well as the cholesterol content of the diet, have usually been singled out in relation to elevated serum liquid levels, within recent years a number of studies have suggested that people with diets rich in fiber have lower blood cholesterol levels.

Leguminous seeds, twice as rich as cereals in fiber content, have been considered in animal experiments [32] and in human subjects [33]. In India, male volunteers ate 247 gm. Bengal gram (chick peas), consuming 16.0 gm. fiber daily. Even while eating a high-fat diet (156 gm. butter fat per day), they had a decrease in mean serum cholesterol from 206 mg. to 160 mg. per 100 ml. [34]. It was necessary to eat the diet for twenty weeks to produce the maximal hypocholesteremic effect. Excretion of all bile salts was significantly increased on the high-fiber diet.

In 1963, a Japanese dietary survey reported [35] an average daily per capita consumption of 5.7 gm. ordinary beans—similar to the United States figure of 7.5 gm.—but a total of 69.4 gm. leguminous seeds, used largely as *miso*, *tofu*, and other processed forms. Since leguminous seeds appear to have a cholesterol-depressing effect, this feature of the Japanese diet may contribute to the maintenance of the low serum cholesterol level characteristic of that population.

Practical considerations for dietary change

It is fortunate that the planning of a vegetarian diet is not difficult. In essence, it is the application of the basic concepts of good nutrition with a relatively few but important modifications. If one were to state the fundamental consideration, it would be to choose a wide variety of foods with a minimum number of refined products. (This basic principle is appropriate to the planning of any type of diet.)

The lacto-ovo-vegetarian diet.—The basic 4 food pattern provides a reliable guide for planning vegetarian diets with the major change in the meat or protein-rich group. In applying the basic 4 pattern to

a lacto-ovo-vegetarian diet, the following recommendations are important:

(a) Since in a vegetarian diet fewer concentrated sources of protein, such as meat, are used frequently, it is necessary to decrease significantly the "empty" calories. It has been estimated [36] that approximately 35 per cent of calories in the typical American diet are from sugars and visible fats. Unrefined foods, on a caloric basis, with few exceptions, supply their quota of protein to the diet. In evaluating the diet of anyone changing from a non-vegetarian to a vegetarian diet, the dilution of nutrients by empty calories should be checked and corrected.

(b) Meat in the protein group will be replaced by a generous intake of a variety of legumes, nuts, meat analogs made from wheat and/or soy proteins, and other formulated plant proteins. Although commercially prepared plant proteins are not essential to a well balanced vegetarian diet, these products do facilitate menu planning and preparation. Their use in the meal replaces the meat entree with little further change in the menu needed. A number of canned, dehydrated, and frozen meat analogs are available in an expanding number of markets. Many combinations, consisting of legumes, cereals, and nuts, with or without milk and eggs, can be made in the home. Vegetarian recipe books are available, and a homemaker can make many tasty vegetarian entrees.

TABLE 5.—CALORIC DISTRIBUTION OF SELECTED FOODS OF ADULT MEN ON VARIOUS DIETS¹

Food	Percent calories		
	Non vegetarian	Lacto-ovo- vegetarian	Pure vegetarian
Milk.....	10.6	16.6	² 2.1
Meat.....	12.9		
Cereal:			
Dark.....	5.5	16.0	13.8
White.....	8.8	4.5	1.4
Legumes.....	1.2	4.0	5.7
Nuts.....	3.4	4.5	15.0
Fruits.....	9.3	19.0	30.8
Fat, visible.....	10.8	8.2	11.3
Desserts (sweets), including honey, sirup, molasses, soft drinks.....	25.0	11.9	7.0

¹ From Hardinge & Stare (6). Similar values were found for women.

² Soymilk.

(c) In the milk group, greater use of nonfat or low-fat milk products, such as cottage cheese, contribute to protein intake and provide vitamin B₁₂. The recommendation of the milk group will supply vitamin B₁₂ sufficient to meet the average adult need.

(d) Since the cereal and bread group also supplies some protein, as well as iron and B vitamins, intake of this group, preferably in the whole grain form, should be somewhat increased. However, care must be observed that this increase does not take place at the expense of the other food groups.

(e) The fruit and vegetable group is usually well represented in the vegetarian diet. Perhaps because of this, a vegetarian diet is often associated in the minds of the general public as consisting largely of vegetables. This class of foods is an important part of the diet, but

other food groups are an integral part of a balanced vegetarian diet.

Actually, the lacto-ovo-vegetarian diet does not differ markedly from the average Western diet. The main difference is that it replaces meat with a variety of legumes, meat analogs, cereals, and nuts and more generous intake of milk and milk products and some eggs. In practice, the nutritional composition of this type of diet is strengthened by the variety of foods which replace meat. Ohlson has pointed out (8) that "many Americans, particularly adult men, eat diets which are poorly balanced because of the large intakes of muscle meat, sweets, and fats and almost complete omission of cereals, except as refined flour entering into the preparation of sweet rolls or desserts. The vegetables and fruits used are limited in both amount and variety."

The pure vegetarian diet.—Several difficulties may be encountered when diets completely devoid of animal foods are eaten. In the first place, many plant foods are low in calories; consequently, the sheer bulk of food to meet caloric needs can become a problem if the selection is not well planned. Second, although a lacto-ovo-vegetarian diet provides adequate amounts of vitamin B₁₂, no presently known practical source of vitamin B₁₂ is present in plant foods. Some individuals appear to maintain good health for many years on a pure vegetarian diet without developing symptoms of deficiency, while others develop symptoms in a shorter time [27]. The reason for this variation is not clear. Until more information is available, a pure vegetarian should include a source of vitamin B₁₂ in his diet.

TABLE 6.—APPROXIMATE NUTRIENT COMPOSITION OF 1-DAY VEGETARIAN DIET

Nutrient	Lacto-ovo-vegetarian	Pure vegetarian	Recommended allowance ¹
Kilocalories.....	2,030	2,040	2,000
Protein (grams).....	78	75	55
Fat (grams).....	76	77	-----
Carbohydrate (grams).....	260	265	-----
Calcium (milligrams).....	1,110	740	800
Iron (milligrams).....	18	24.8	18
Vitamin A (International units).....	12,600	14,600	5,000
Thiamin (milligrams).....	2.5	2.9	1.0
Riboflavin (milligrams).....	2.2	2.3	1.5
Niacin (milligrams).....	18.6	22.9	13.0
Ascorbic acid (milligrams).....	185	185	55

¹ For woman, 22 to 35 yr of age.

The following recommendations are important in changing from a lacto-ovo-vegetarian diet to a pure vegetarian diet:

The same consideration for the protein and cereal-bread groups which has already been made applies to a pure vegetarian diet. There will be, of course, increased use of the foods of these two groups, as well as from the fruit-vegetable group, to meet caloric needs. An adequate intake of calories is important. When caloric intake is inadequate, the body will preferentially use protein to meet its energy needs.

The milk group requires special attention. In the lacto-ovo-vegetarian diet, the milk group supplies 75 percent of the calcium, 43 percent of the riboflavin, 22 percent of the protein, and practically 100 percent of vitamin B₁₂. One way to obtain an adequate intake of these nutrients is to use sufficient quantities of fortified soybean milk.

For an adult, this would be a minimum of two glasses a day. The label must be checked to make certain that the soybean milk is fortified.

Green leafy vegetables, on a weight basis, supply as much calcium and riboflavin as milk (table 4). A large serving (about 1 cup, 200 gm.) of such greens as collards, kale, turnip, and mustard, provides as much calcium as 1 cup milk. It is interesting that the Chinese Medical Association [37] recommended an intake of 500 gm. green leafy vegetables per day. In addition to greater consumption of dark green leafy vegetables, the use of cabbage, broccoli, and cauliflower will contribute lesser amounts of calcium but more than most other vegetables. Other plant sources which are fair to good sources of calcium include: legumes, particularly soybeans; some nuts, particularly almonds; and dried fruits. An evaluation of a pure vegetarian diet must be made to determine how often and in what quantity these plant sources are used. Occasional use cannot be counted on to replace the calcium and riboflavin of milk.

TABLE 7.—AMINO ACID CONTENT OF 1-DAY LACTO-OVO-VEGETARIAN AND PURE VEGETARIAN DIETS

[In grams]

Amino acid	Lacto-ovo-vegetarian	Pure vegetarian	Minimum	Recommendation ¹
Isoleucine.....	3.74	3.10	0.7	1.4
Leucine.....	6.59	5.66	1.1	2.2
Lysine.....	3.39	4.09	.8	1.6
Methionine.....	1.36	1.08	-----	-----
Cystine.....	1.15	1.27	-----	-----
Total sulphur.....	2.51	2.34	1.1	2.2
Phenylalanine.....	4.13	3.76	-----	-----
Tyrosine.....	3.10	2.56	-----	-----
Total aromatic.....	7.23	6.32	1.1	2.2
Threonine.....	2.93	2.75	.5	1.0
Tryptophan.....	.92	.89	.25	.5
Valine.....	4.34	3.74	.8	1.6

¹ For average man.

Hardinge and Stare found [6] that diets of the pure vegetarians they studied usually consisted of cooked cereals and bread, legumes, nuts, large quantities of fruits and vegetables, especially large salads, vegetable oils, and olives. Minimal quantities of refined and commercially prepared foods were used. Few desserts were eaten. Table 5 shows the caloric distribution of selected foods from their study.

Properly selected lacto-ovo-vegetarian diets are tasty and attractive and require no supplementation. A pure vegetarian diet can be planned that is adequate in quantity and quality of protein, as well as all other known nutrients, if supplemented with vitamin B₁₂. The approximate values of certain essential nutrients and amino acids for a one-day vegetarian diet are given in tables 6 and 7.

The dimensions of change in food patterns and products, in attitudes and habits during the 1960's have been extensive. The seventies and eighties will continue to present challenges to the dietetic practitioner to become concerned and involved in meeting the nutritional needs of the changing life style of our contemporary world.

1-day vegetarian

BREAKFAST	NOON MEAL	EVENING MEAL
Orange juice—4 oz.	Soy patties with tomato sauce—2	Vegetable soup—1 c. (200 gm.)
Cooked oatmeal—1 c.	Baked potato—1	Sandwich
Milk (LV) ¹ —4 oz.	Margarine—1 pat	whole wheat bread—2
Soymilk (PV) ² —4 oz.	Cooked fresh or frozen peas— $\frac{2}{3}$ c.	slices
Whole wheat toast—1 slice	Shredded carrot salad— $\frac{1}{2}$ c., scant	garbanzo - egg filling (LV)
Peanut butter—Tbsp.	Dressing— $\frac{1}{2}$ Tbsp.	Savory garbanzos (PV)
Clear hot cereal beverage, if desired	Wheat roll	Sliced peaches— $\frac{1}{2}$ c.
	Margarine—1 pat	Walnut stuffed dates—4
	Strawberries, fresh or frozen without sugar— $\frac{3}{4}$ c.	Milk (LV)—8 oz.
	Milk (LV)—8 oz.	Soymilk (PV)—8 oz.
	Soymilk (PV)—8 oz.	

¹ LV=lacto-ovo-vegetarian.² PV=pure vegetarian.

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A NUTRITION AUTHORITY DISCUSSES MRS. E. G. WHITE

(By Clive M. McCoy, Ph. D., Professor of Nutrition, Cornell University)

The fascination of history is the never-ending discovery of remarkable people to whom one is deeply indebted for advances in knowledge. One seldom comes to know about such people suddenly. Like living acquaintances, he first meets them at various places. Gradually he comes to know them more intimately and studies their lives and writings in detail. This is particularly true as regards the people one meets in studying the history of nutrition.

For the past quarter of a century I have taught a course for graduate students on the history of foods and nutrition. In this course are presented original materials, starting with the early Greek work by Athenaeus who lived in Rome at the end of the second century A.D. Down through the succeeding centuries notable names appear. For example, in the middle of the thirteenth century Petrus Hispanus published much about diet. Shortly after the discovery of America one of the greatest books about nutrition and old age was written by

Luigi Cornaro (1464–1566). Later centuries, on down to the twentieth, provides a remarkable array of books that present the theories, and sometimes the research, of the writers, on the broad subject of nutrition and foods. Such historical works must be scrutinized critically, for they contain much that is not true. In fact, most of these works are a curious mixture of truth and error.

Among the thousand historical acquaintances in my files, one of the most worth-while is Ellen G. White. As near as one can judge by the evidence of modern nutritional science, her extensive writings on the subject of nutrition, and health in general, are correct in their conclusions. This is doubly remarkable: Not only was most of her writing done at a time when a bewildering array of new health views—good and bad—were being promoted but the modern science of nutrition, which helps us to check on views and theories, had not yet been born. Even more singular, Mrs. White had no technical training in nutrition, or in any subdivision of science that deals with health. In fact, because of her frail health from childhood she completed only a part of a grammar school education.

OBTAINED E. G. WHITE BOOKS

I do not know when I first heard of Mrs. White. While a college student I worked for a few weeks in a machine shop in Battle Creek, but I cannot recall her name from that period. From time to time I have had visits from a few Adventist physicians and have come to admire them for their sincerity in service and interest in nutrition. Gradually through the years, and more particularly in recent times, I have acquired a number of Mrs. White's writings.

However, my knowledge of the wisdom of Mrs. White has only begun, and the following notes must be considered as very incomplete and inadequate.

In order to place her health teachings in the proper perspective. I must first set down briefly certain historical facts.

Until modern times men lived in rather restricted areas of the earth, because they could not travel far nor rapidly. Men in each area were adjusted to the foods available. A physician in England has written an interesting summary of this relation of man to available foods under the title "The Neglect of Natural Principles in Current Medical Practice" (*Journal of Applied Nutrition*, 1958, 11, 116).

All plants and animals that serve as food for man and other animals have long been known to be very complex mixtures, often combined into hundreds of semi-living compounds called enzymes. Some of the organic compounds can be made by the body of man. Many are made by plants, but are essential for the animal body. Without such compounds, vitamins, essential amino acids or fatty acids, the animal body sickens and dies.

MAN'S DIET IN EARLIER AGES

In earlier ages man did not destroy the complex nutrients of natural foodstuffs, because his supply was often marginal and he had to eat the whole product in the form in which it grew. Cookery was probably the first method evolved that tended to destroy part of the vita-

mins of food. However, early man was migratory, within limits, and often had little fuel available. Hence he cooked briefly as many Eastern people do today, because of limited fuel supplies. Early man learned to sprout certain seeds such as soy beans that are difficult to eat without long cookery. Sprouting conserved the natural food values and made short-time cookery possible.

Man first learned to destroy most of the value of natural foods when he discovered the distillation of alcohol, more than a thousand years ago, and when he learned to crystallize sugar, about two thousand years ago. Distillation and crystallization are human methods of removing most of the vitamins and other essentials of natural foods. When grain, such as corn, is fermented and then distilled, all of the protein, fats, vitamins, and minerals are left in the retort. Today these essentials are fed to animals, and man drinks the alcohol in the form of vodka or whisky. When sugar cane or sugar beets are grown they are rich in many essentials, like other foods, but crystallizing out the sugar leaves the essentials behind, just as much as does distillation.

MODERN SCIENTIFIC ERA

Until modern times these processes had little importance in human nutrition, because man could not work on a large scale to produce thousands of tons of alcohol and sugar. He lacked the equipment for large scale processing. Furthermore, he had no means of assembling the ingredients for making sugar or alcohol on a vast scale, even if the natural foods could have been grown in large amounts. Two hundred years ago a bill to restrict the growth of London was debated in Parliament because of the difficulty of transporting sufficient food to the people by means of horses and carts. In past ages the amounts of alcohol and sugar that were produced were small enough to make these products luxuries.

About 150 years ago the sciences of chemistry, physics, and physiology started to advance rapidly. These sciences finally made it possible to produce and distribute the vast array of foods that flood the American market today. At the same time they made it easy to produce and sell huge amounts of highly processed materials such as sugar and alcohol that appeal to the taste of man but may lead him downward in well-being. Today, increased means of communication such as the television and a growth in the knowledge of the psychology of selling make it possible to sell man ever-increasing amounts of these deteriorated products.

With the development of the natural sciences came a better understanding of human nutrition. The chemist gradually, in the course of the past 150 years, came to appreciate that natural foodstuffs were composed of numerous essentials such as minerals, amino acids, protein, and unsaturated fatty acids. However, this growth of scientific knowledge has not insured man against malnutrition and ill health, because such knowledge is very incomplete. Hence even today human nutrition must rest upon experience and the teaching of the past.

As the basic knowledge of nutrition advanced, men set up standards that purported to show what every person should consume if he desires to be healthy and well fed. The first of such standards was set up by a chemist named Prout, more than a century ago. The most recent of

these was formulated by various health agencies—scientific and governmental—in different countries.

Even today, such standards are merely rough guides and are very incomplete because we know so little about human nutrition. Ingesting foods to provide all of the nutrients of these standards will not insure freedom from malnutrition today, any more than it would a hundred years ago.

In some respects such standards have had a very bad influence, because the teachers of nutrition make their pupils think that there can be no malnutrition in a nation whose people consume foods that provide the levels of vitamins or compounds suggested in these standards. Such teaching gives free rein to those who sell alcohol, soft drinks, sugar, and refined products to increase their business, because they can constantly assert that the people are fed adequately.

Nutritional scientists who worship at the shrine of so-called standards have been equally inconsistent from the beginning. A century ago the disease pellagra was common in America and some of the corn-eating areas of Europe. About this time the disease was eliminated from France by decreasing the amount of corn consumed and having the people eat more milk, eggs, and meat. The French chemist, Rousset, knew how to prevent pellagra as early as 1840, but more than seventy years were to pass before Americans made use of this knowledge. The nutritional standards of the pellagra era would have made man think he was adequately fed. The truth was the opposite.

Today the same condition exists, in principle, in America. The exponents of the standards assert that Americans are the best fed in the world. At the same time thousands of Americans are dying from the disease of heart and arteries. There is growing and impressive evidence that these diseases are the reflection of bad diet, but they occur in those who abide by the so-called adequate nutritional standards, which fact forces us to admit that the whole science is still too primitive to provide wholly adequate guidance, even though much is known.

Health has been a matter of little individual concern to most people in our nation during its whole history. Among the 170 million people in America today there are probably not more than 10 million who are willing to devote substantial thought and self-discipline to maintain healthy bodies. Only after they have lost their health are most people willing to give any attention to the care of their bodies.

While the selection and preparation of food plays a key role in the maintenance of health, few people select food on the basis of its nutritive value. Most select it on the basis of its taste, the way the product is packaged, the pressure of advertising, or the ease of preparation. Hence, the large food processors orient their research programs toward packaging, taste, and convenience rather than toward nutritive value.

A sound nutrition program takes account of more than just the purchase of food. A healthy body, a satisfactory program of living, and a tranquil mind are all part of the essentials for sound nutrition, since the glands that insure digestion and assimilation of food cannot function when under the influence of a disturbed mind.

I have given this brief summary to provide the setting for my comments on the teachings of Ellen G. White, particularly in terms of

the usefulness of her teaching today for the population of America. Whatever may be the reader's religion, he can gain much in the midst of this confused world in which we live, by a study of the writings of Mrs. White. Also, every thoughtful modern nutritionist must be impressed by the soundness of Mrs. White's teachings in spite of the fact that she began to write nearly a century ago.

Only a small fraction of people seem to grasp the importance of the concept of "balanced living" or the "wholeness" of life. This is expressed very well in the small compilation of writings by Mrs. White that are included in "From City to Country Living". In this age, when problems of crime and juvenile delinquency are ever increasing, her writings have special interest to the sociologist. But to the modern nutritionist they also have special appeal because vast numbers of people have now moved to the edge of cities. They have facilities for producing much of their own vegetables and fruits with a minimum of poisonous spray residues. They have the space to grind their own wheat and make their own bread. They can even raise their own potatoes and squash. Mrs. White understood the value of such foods for better nutrition, and the value of the experiences of gardening as human recreations.

When one reads such works by Mrs. White as "Ministry of Healing or Counsels on Diet and Foods" he is impressed by the correctness of her teachings in the light of modern nutritional science. One can only speculate how much better health the average American might enjoy, even though he knew almost nothing of modern science, if he but followed the teachings of Mrs. White.

To understand better the remarkable nature of her teachings, we should study them in the setting of the intellectual climate that prevailed during the earlier years of her life. This climate provided her with the problems that needed answers. Some of the problems press for solution even more today, because of the greater complexity of living and the very great increase in the world populations.

AN EXPLANATORY NOTE

The background of Dr. Clive M. McCay's articles is an interesting one. Some years ago he came into possession of one of Mrs. White's books on the subject of health. He was impressed with what he read, particularly because the history of foods and nutrition was subject to which he had given special study. The question came at once to his mind: How did this woman know so much about nutrition in a day when so many unfounded views were abroad? In time he acquired several more of her books and was increasingly impressed.

Then one evening last year he was invited to give a talk to a men's club of the local church he attended. He chose for his subject: "An Unusual Nineteenth-Century Woman, Mrs. E. C. White." A copy of his talk reached our desk. On a trip last summer we stopped at Cornell University, in New York State, to visit Dr. McCay. We found him exactly where we might have expected to find him—hidden away in an office that was surrounded by countless rats and mice whose contribution to nutritional science was matched by the oppressive odor they gave forth.

Dr. McCay is a classic exhibit of the truly scientific man. He was wholly undisturbed by the malodorous rodents. In fact, he was enthusiastic about them, pointing to this and that small creature that was eating, sleeping, waking, in a small metal cage for the great good of science. He then took us out to one of the nearby university farms. There a large barn with adjoining pens marked "Dr. McCay's laboratory" contained various animals that spend their days in munching different kinds of food to provide data on the effects of various diets. We might add that Cornell, one of America's leading universities, has done a great deal of significant research work in nutrition.

We stayed overnight at Dr. McCay's home, a very livable, rambling, remade farmhouse. We soon discovered to our delight that though he was a specialist in the field of nutrition, his active interest and reading extended over a remarkable range. More than one during the evening he returned to the question. "How do you explain the fact that Mrs. White, with very little formal education and no special training in nutrition, so accurately set forth nutrition principles that are only now scientifically established?" He ruled out as wholly unsatisfactory the answer sometimes casually given: "Mrs. White simply borrowed her ideas from others." He observed that such an answer simply raises another question: "How would Mrs. White know which ideas to borrow and which to reject out of the bewildering array of theories and health teachings current in the nineteenth century?"

Dr. McCay did not attempt to answer such questions. As a scientist he was interested in the phenomenon of her singular knowledge in advance of scientific discovery and experiment. Nor did we seek during the delightful but all too brief visit to enter into extended discussion of the theological doctrine of inspiration. We simply stated that Adventists accept Mrs. White's declaration that she was inspired of God, and let the matter stand.

Dr. McCay was ready and happy to respond to our invitation to him to write something for *The Review and Herald*. The series from his pen, here reprinted, presents the essence of his address to the men's club, plus additional relevant material.

—F. D. NICHOL.

SCIENCE CONFIRMS ADVENTIST HEALTH TEACHINGS

(By Clive M. McCay, Ph. D., Professor of Nutrition,
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To understand rightly the great need for dietary reform that existed at the time Mrs. White began to write, let us note the kind of foods available to the average family during the first part of her life—that is, from 1827 to the outbreak of the Civil War in 1861. During that period the typical farm family—and most families lived on a farm, from Maine to Indiana—had some chickens, swine, sheep, and a few cows. The housewife looked after the garden and the chickens while the husband labored in the field. The diet was reasonably satisfactory from the time rhubarb checked latent scurvy in April until most of the fresh foods had disappeared by Thanksgiving.

From Thanksgiving until Easter the diet grew progressively worse, with outbreaks of disease in February and March. Although the French scientist Appert patented methods for canning food in 1810, housewives had no containers for doing this until more than a half century later. Therefore, they had to depend upon drying apples, sweet corn, peas, and beans over the kitchen stove. Vinegar was available because the common fruit was apples. Salt was the other common preservative. Most meat was salted and smoked, although pork was often fried and stored in earthenware jars with the meat sealed and sterilized by pouring hot lard over it. Pickles could be preserved, and families of Germanic origin made sauerkraut.

Walnuts, hickory nuts, and in some areas, chestnuts, were available. Salted fish was commonplace. Eggs were plentiful in summer and scarce in winter because there was no good way to preserve them, except by storage in lime or sawdust.

Cellars preserved the potatoes and apples, although the potatoes were often nearly exhausted by spring.

The Indiana children took corn bread for their lunch at school until well after the middle of the century. At home they had much corn-meal mush and hominy. Highly refined white flour did not become common until after the middle of the century, because the roller mills that could take out the germ and the vitamins from wheat flour were invented only about the middle of the nineteenth century.

Butter could be stored in crocks, but was usually quite rancid.

Foods bought at the country stores usually consisted of salt fish or salt meat, some coffee or tea, some sugar, and a jug of thick molasses. Since the molasses came north from New Orleans, the supply was cut off during the sixties, and areas like Indiana developed a taste for the sour sorghum molasses.

Well before the birth of Mrs. White there were a few Americans protesting the bad diet, the smoking, and the drinking. Even from early antiquity there had been groups outside the Jewish traditions that subscribed to vegetarianism. Sylvester Graham, who was born in 1794, stirred the young American nation with his lectures advocating vegetarianism, the improvement of bread, the abolishment of alcoholic beverages, and more healthful living. He had much influence during the first half of the nineteenth century, but left no permanent group of followers. The vegetarian church was founded in Philadelphia in 1817, but it soon disbanded.

About 1840 the Shakers stopped the use of pork, strong drink, and tobacco. Many turned to vegetarianism. Their rules of health included the following:

1. Supply at least one kind of coarse-grain bread per meal. Avoid cathartics.
2. Have the sickly and weakly cease using animal foods, especially fats.

3. Keep the skin clean by regular bathing. But the Shakers reached their peak about 1850 and have now—thanks to their celibate views—almost perished.

In Mrs. White's "Life Sketches" one learns much about both the bad food served in most homes and the toll of diseases that resulted. It is no wonder that the relationships between food and diseased people were deeply impressed upon the Whites as they traveled in New England and the Middle West a hundred years ago. The diet was a monotonous one of fat, salted meats, bread, potatoes, and butter. No wonder that Elder White developed dyspepsia. Poverty, then common, served to make the fare even more meager.

When foods were available the Whites were plagued by poverty, yet they kept their determination to remain free from debts. In 1847 Mrs. White wrote, "I allowed myself and child one pint of milk each day. One morning before my husband went to his work, he left me nine cents to buy milk for three mornings. It was a study with me whether to buy milk for myself and babe or get an apron for him. I gave up the milk, and purchased the cloth for an apron to cover the bare arms of my child."—*Testimonies*, vol. 1, p. 83.

In 1852, when the Whites lived in Rochester, they had so little money that they could not afford potatoes and butter, but ate turnips and sauce.

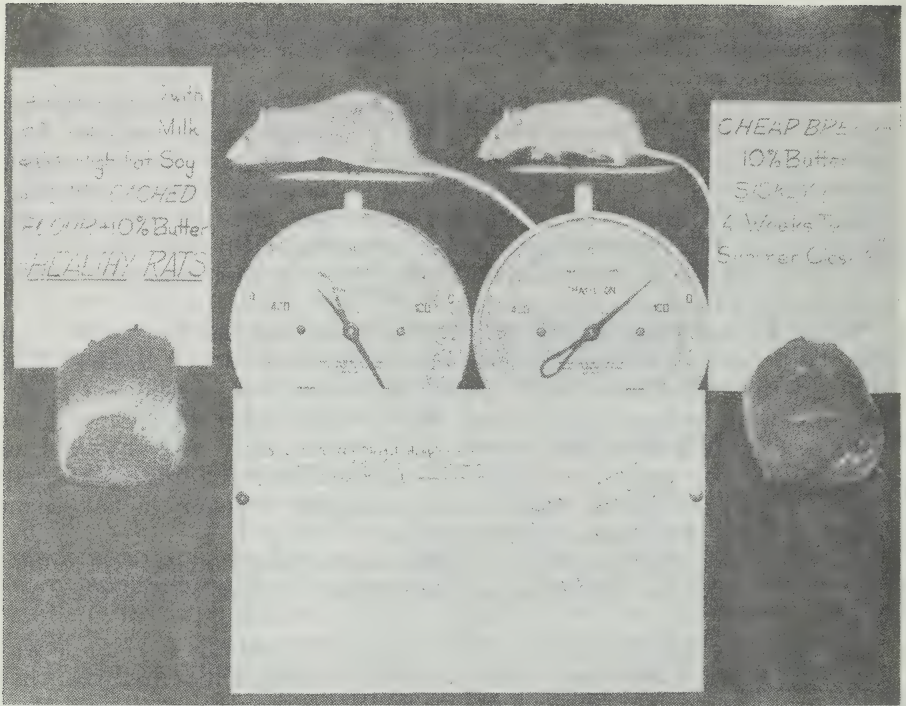
At this time meals at hotels cost twenty-five cents. Hard liquor was five cents extra. Many men paid the extra, although it is doubtful that the per capita consumption of alcoholic beverages was equal to that of today, since few women drank. Although cigarettes were not to become accepted until much later, there was much smoking and chewing of tobacco on the steamers and in the public waiting rooms.

The Whites in their travels must often have thought, in the words of Pascal, that "nothing more astonishes me than to see that men are not astonished at their own weakness."

SPECIFIC ILLUSTRATIONS

So much by way of background. I earlier stated that Mrs. White was a remarkable woman, particularly in terms of her health views. I wish, now, to be specific, in support of this statement, by comparing certain of her teachings with present-day well-established facts on nutrition. Though, for convenience, I shall quote, in part, from her book "The Ministry of Healing," first published in 1905, most of what she there sets forth was presented in various of her writings of much earlier days.

Today there is a widespread movement to reduce the intake of fats, especially animal fats, in order to reduce the blood cholesterol and the dangers of atherosclerosis. Mrs. White wrote, "Nut foods are coming largely into use to take the place of flesh meats. * * * When properly prepared, olives, like nuts, supply the place of butter and flesh meats. The oil, as eaten in the olive, is far preferable to animal oil or fat."—"The Ministry of Healing," p. 298.



An exhibit of the research work done by Dr. Clive M. McCay at Cornell University. Note the marked difference between the two rats. The one at the left was fed on "good bread"; the one at right on "cheap bread."

Near the end of Mrs. White's life in 1915 men began to appreciate that the milling of white flour removed most of the vitamins, part of the protein, and the important trace minerals such as iron. However, even nutritional authorities were very slow to inveigh against white bread. Today nutritionists know that these vital constituents are lost when the bran and germ are taken from the wheat. Mrs. White wrote, "For use in bread-making, the superfine white flour is not the best. Its use is neither healthful nor economical. Fine-flour bread is lacking in nutritive elements to be found in bread made from the wholewheat."—*Ibid.*, p. 300.

In spite of her emphasis upon a given type of diet, Mrs. White appreciated that there were some people who could not tolerate foods that were well suited to the majority. Today it is well recognized that there are a few people with very sensitive intestines that suffer if the diet has much fiber. Mrs. White wrote, "Foods that are palatable and wholesome to one person may be distasteful, and even harmful, to another. Some cannot use milk, while others thrive on it. * * * For some the coarser grain preparations are good food, while others cannot use them."—*Ibid.*, p. 320.

DANGER OF OVEREATING

Today it is well recognized that overeating and overweight produce much ill health. This is one of the few areas in which all professional nutritionists agree. Mrs. White wrote, "There should not be a great variety at any one meal, for this encourages overeating and causes indigestion."—*Ibid.*, p. 299. "Abstemiousness in diet is rewarded with mental and moral vigor." "At each meal take only two or three kinds of simple food, and eat no more than is required to satisfy hunger."—*Ibid.*, pp. 308, 310.

Throughout the whole period spanned by Mrs. White's life it was customary to eat elaborate meals upon the weekly holy day. She wrote, "We should not provide for the Sabbath a more liberal supply or a greater variety of food than for other days. Instead of this the food should be more simple, and less should be eaten in order that the mind may be clear and vigorous to comprehend spiritual things."—*Ibid.*, p. 307. All thinking people will agree with this today, though many fail to practice it.

Today many people are restricting their use of salt in order to lower their blood pressure or in the hope of preventing high blood pressure. Attempts are made to keep the sodium intake low by using baked products made with yeast instead of baking powder. Mrs. White wrote, "Do not eat largely of salt." "The use of soda or baking powder in breadmaking is harmful and unnecessary."—*Ibid.*, pp. 305, 300.

Today we teach home economics throughout our whole nation. Mrs. White wrote, "Cooking is no mean science, and it is one of the most essential in practical life. It is a science that all women should learn. * * * To make food appetizing and at the same time simple and nourishing, requires skill."—*Ibid.*, pp. 302, 303.

Meals served in many courses have almost passed from the American home, due probably to the disappearance of maids rather than a comprehension of Mrs. White's philosophy that all food should be put on the table at once, instead of in courses, so that one will know what is available and not overeat. (See "The Ministry of Healing", p. 306).

ADVENTIST HEALTH TEACHINGS FURTHER CONFIRMED

(By Clive M. McCay, Ph. D., Professor of Nutrition,
Cornell University)

A problem of much concern in America today is that children insist upon watching television and eating snacks in the late evening. They then arise too late in the morning to eat breakfast. Before noon they are tempted to eat snacks and thus spoil their lunch. Mrs. White wrote: "Irregularities in eating destroy the healthful tone of the digestive organs, to the detriment of health and cheerfulness. And when the children come to the table, they do not relish wholesome food; their appetites crave that which is hurtful for them."—"The Ministry of Healing," p. 384.

Every thinking person today would agree with such wise statements of Mrs. White as, "Pure air, sunlight, abstemiousness, rest, exercise, proper diet, the use of water, trust in divine power—these are the true remedies."—*Ibid.*, p. 127. "Parents should early seek to interest their children in the study of physiology and should teach them its simpler

principles. * * * An education in the things that concern life and health is more important to them than a knowledge of many of the sciences taught in the schools."—*Ibid.*, pp. 385, 386.

Or take these statements:

"The best food for the infant is the food that nature provides. Of this it should not be needlessly deprived."—*Ibid.* p. 383. "In the entertainment of guests there should be greater simplicity."—*Ibid.*, p. 322. "Where wrong habits of diet have been indulged, there should be no delay in reform."—*Ibid.*, p. 308. "Take active exercise every day, and see if you do not receive benefit."—*Ibid.*, p. 310. "One of the surest hindrances to the recovery of the sick is the centering of attention upon themselves."—*Ibid.*, p. 256.

Mrs. White wrote:

"There is a large class who will reject any reform movement, however reasonable, if it lays a restriction upon the appetite. * * * By this class, all who leave the beaten track of custom and advocate reform will be opposed, and accounted radical."—"Counsels on Diet and Foods", p. 195.

Today this class is greatly strengthened in its opposition by the tremendous forces of advertising and the mass control of activities as described in such works as that of Vance Packard in "Hidden Persuaders." Hence, improvement of the diet of people is probably far more difficult than it was in the time of Mrs. White.

THE EVILS OF SMOKING

Today most of us tolerate the smoke blown in our faces as we travel by air, and we try to avoid getting holes burned in our clothing as we ride with cigarette smokers on hotel elevators. Today the press is filled with stories relating to smoking—because they force increases in the advertising budgets of the tobacco companies—in an attempt to offset the truthful disclosures. Recent impressive research seems to point to a definite relationship between smoking and disease of the heart and blood vessels, to say nothing of its relationship to lung cancer. Mrs. White wrote, "Tobacco is a slow, insidious, but most malignant poison. * * * It is all the more dangerous because its effects are slow and at first hardly perceptible."—"The Ministry of Healing," pp. 237, 328.

Mrs. White recognized the value of mixing a variety of grains. She wrote: "All wheat flour is not best for a continuous diet. A mixture of wheat, oatmeal, and rye would be more nutritious than the wheat with the nutrifying properties separated from it."—"Counsels on Diet and Foods," p. 321. She recognized the truth from Ezekiel, "Take thou also unto thee wheat, and barley, and beans, and lentiles, and millet, and fitches, and put them in one vessel, and make thee bread thereof" (Ezekiel 4:9). These additions supplement the proteins of wheat bread, as well as increase such essentials as calcium.

In his book, "The Geography of Hunger," Josue de Castro has stressed the fact that millions of people in the world are suffering from malnutrition because of poor dietary practices. In parts of the world this is owing to the few foods that are available. In the United States it is caused by the great surplus and poor selection owing to ignorance and the pressures of commercial industries that seek to force their products upon the public by subtle methods of advertising. The people

of the world would serve themselves best if they produced part of their foods in their own gardens and if they followed a general plan of a wise leader such as Mrs. White.

Among nutritionists there is an acute awareness of the problem of feeding the ever-increasing population of the world. This has been well summarized recently in the *Journal of the New York Academy of Sciences* in an article by J. G. Harrar entitled "Food, Science and People." He notes the increase in the population of the earth from a half billion in the year 1700 to five times this number in 1950. It is hazardous to venture a guess as to what the future holds in regard to population growth, because many developments are in the offing that may reverse the whole trend. Large numbers of chemicals are finding their way into the human food supply in the form of additives, spray residues, drugs fed to poultry and meat animals, as well as radioactive-fallout materials such as strontium-90. Chemists are well on their way in developing compounds that will produce sterility when added to food supplies.

FOOD VALUE LOST IN MEAT

These and many unanticipated events may check or destroy the human population. However, if this population grows at the present rate basic changes are inevitable. When man feeds an animal such as a pig or a turkey upon the grains that he can eat, at least three fourths of the food value is lost. In other words four men can live upon plant foods directly, in comparison with the one man that can be fed if the food is first converted into meat and then consumed by man.

Mrs. White well stated that "The life that was in the grains and vegetables passes into the eater. We receive it by eating the flesh of the animal. How much better to get it direct, by eating the food that God provided for our use!"—*The Ministry of Healing*, p. 313.

Man cannot eat much grass and hay, so the cow serves us in changing this to milk. However, the chemists are busy taking out of hay such products as the protein, so it can be eaten by man. Methods are being devised to break down the cellulose in plants so it can be digested by man. Each day in Wisconsin many tons of yeast are made from the wastes of paper mills. Yeasts are among the simpler plants that are readily digested by man. Yeasts are among the richest foods in vitamins and protein.

As the population of the earth grows very great most people will have to turn largely to vegetarian diets. Furthermore, as the demand increases for grains for cereal foods, man will no longer be able to afford the luxury of alcoholic beverages. At present grains are fermented and the alcohol is distilled off. The valuable food residues of vitamins, protein, and minerals are now fed to animals to produce meat, milk, and eggs. In order to feed large populations, alcohol production will have to cease, since it involves the use of grains that can be eaten by man.

Likewise, as food becomes scarce man will no longer be able to afford the luxury of wasting land in the production of tobacco. Usually this is rich land for growing grains.

There is no basis for believing that these changes to universal vegetarianism, to the cessation of making alcohol, and the growing of tobacco will occur within our lifetime, but certainly they may be expected within a century unless vast numbers of people are killed, or the growth of the population is checked. At present our problem is

to discipline ourselves in our food habits and ways of living in order to ensure optimum health.

In some respects it might be easier to write about the areas in which nutrition specialists and the writings of Mrs. White may seem to disagree, because the area is so much smaller. These areas are probably owing to changes in food technology. The raw milk in the days of Mrs. White was a carrier for many contagious diseases, such as tuberculosis, dysentery, and typhoid fever. This may explain, in turn, why she declared that cheese was not a satisfactory food. Perhaps on the same basis we should understand her further statement: "The use of milk [in bread] is an additional expense, and it makes the bread much less wholesome."—*Ibid.*, p. 301. Products like dry skim milk, now used in bread making, were unknown in the lifetime of Mrs. White. Skim milk was fed to the pigs in her day. It contains the most important nutrients of the milk in terms of calcium, protein, and vitamins.

DISCUSSION SUMMED UP

To sum up the discussion: Every modern specialist in nutrition whose life is dedicated to human welfare must be impressed in four respects by the writings and leadership of Ellen G. White.

In the first place, her basic concepts about the relation between diet and health have been verified to an unusual degree by scientific advances of the past decades. Someone may attempt to explain this remarkable fact by saying: "Mrs. White simply borrowed her ideas from others." But how would she know which ideas to borrow and which to reject out of the bewildering array of theories and health teachings current in the nineteenth century? She would have had to be a most amazing person, with knowledge beyond her times, in order to do this successfully!

In the second place, everyone who attempts to teach nutrition can hardly conceive of a leadership such as that of Mrs. White that was able to induce a substantial number of people to improve their diets.

In the third place, one can only speculate about the large number of sufferers during the past century who could have had improved health if they had accepted the teachings of Mrs. White.

Finally, one can wonder how to make her teachings more widely known in order to benefit the overcrowded Earth that seems inevitable tomorrow with the present rate of increase of the world's population.

In spite of the fact that the works of Mrs. White were written long before the advent of modern scientific nutrition, no better over-all guide is available today.

[Reprinted from *The Review and Herald*, Aug. 7, 1958]

ARE NONFLESH PROTEINS ADEQUATE?

A SCIENTIST'S REPORT ON SOME INTERESTING RESEARCH

(By U. D. Register, Ph. D.)

The subject of the quality and quantity of protein needed in the diet has been intensively studied since the days of Liebig (mid-nineteenth century), who thought that protein was the source of energy for work. This view led to the conclusion that the more one works the more pro-

tein he requires. But it is now known that protein requirements are not increased by activity (*Am. J. Pub. Health* 33:1444, 1943). The German physiologist Voit, a contemporary of Liebig, recommended 118 grams of protein a day. He based this recommendation simply upon a survey of the average intake of protein by German workers.

Present-day research, based on controlled experiments, shows that the minimum requirement is much less. In 1946 outstanding investigators at Harvard and the University of Illinois reported that the minimum requirement for adult men was approximately 30 grams of protein per day, whether the diet was of plant origin or from a mixture of plant and animal foods (Sahyun, "*Proteins and Amino Acids in Nutrition*" [1948], p. 159). As late as 1955, Dr. W. C. Rose of the University of Illinois, for more than 25 years outstanding in the field of protein research, concluded that the protein requirement of adult men was less than 25 grams per day (*J. Biol. Chem.* 217: 997, 1955).

On a diet containing a fair variety of natural foods—for example, fruits, grains, nuts, vegetables, milk—a person who eats an adequate total of calories cannot fail to secure at the same time an adequate amount of protein. For example, studies by Dr. Mervyn Hardinge of the College of Medical Evangelists revealed that the average daily consumption of protein by men and women living on an exclusively plant diet was 83 grams for men and 61 for women; on a lacto-ovo-vegetarian diet, 98 for men and 82 for women. (*J. Clin. Nutrition* 2:73, 1954). This study, conducted under the direction of Dr. Frederick J. Stare of Harvard University, indicates that the average man and woman on these nonflesh diets obtained more than 100 per cent above what nutritional authorities declare is the minimum daily protein requirement.

Nutrition surveys that were made in Europe after the second world war revealed that no protein deficiency occurred when 95 to 100 per cent of the protein came from cereal grains and potatoes, if adequate supplies of these foods were available. Only those on starvation diets showed any protein deficiency, and their condition improved simply by giving them more of the simple food such as grains and potatoes. In summarizing these surveys, Hegsted and Stare of Harvard stated that it is most unlikely that a protein deficiency will develop in apparently healthy adults on a diet of cereals and vegetables, provided these are available in adequate amounts (*J. Lab. & Clin. Med.* 31:26, 1946). Therefore; as long as man has enough to eat, there is not likely to be a deficiency in the average total protein intake.

The National Research Council has recommended 65 grams of protein per day for the average man and 55 for the average woman. These allowances provide a liberal margin of safety, in terms of studies at Harvard, Illinois, and Minnesota (*J.A.M.A.* 138:503, 1948). The Harvard investigators declare that the allowance is most generous and could, if necessary, be reduced to 50 grams and still provide approximately 30 per cent margin above requirement (*J. Lab. & Clin. Med.* 31:261, 1946).

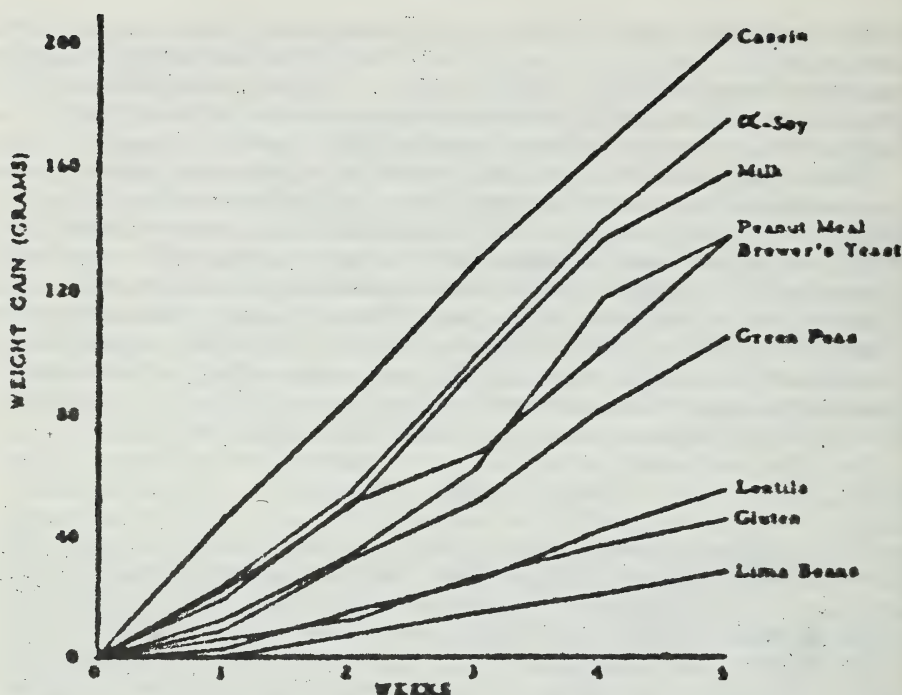


FIGURE 1.—Growth response of rats on single sources of protein at an 18 percent protein level. The diets contain adequate amounts of the proper nutrients to maintain normal growth of the albino rat, only the source of the protein portion being altered. Casein is from milk, α -soy is an isolated soy protein, gluten is from wheat.

The ease of obtaining 100 per cent above the minimum protein requirement is also seen in countries where the diet may be primarily from plant sources. If people in India were eating as many calories as those in the United States, their daily consumption of protein would be more than 77 grams per day even though about 90 per cent of the protein is from plant origin (C. E. KELLOGG, "Food, Soil and People," *UNESCO* 8, 1950).

In view of present-day experiments it is interesting to note a statement recently made by a professor at the University of Michigan concerning the influence of early research workers as to protein requirement: "No one can deny that Liebig and Voit were great investigators, but the errors of great men are a hundred times more dangerous than the nonsense of multitudes. Thus the agitation in favor of meat has been disseminated throughout the world."—H. B. LEWIS, *J. Am. Dietet. A.* 28:702, 1952).

Certain proteins, when fed alone, will support growth and maintain body functions, whereas others will not. The explanation is that some proteins contain all the known amino acids, or building blocks, for these functions, whereas others do not. About 20 amino acids are found in most proteins in varying amounts. At least eight of these

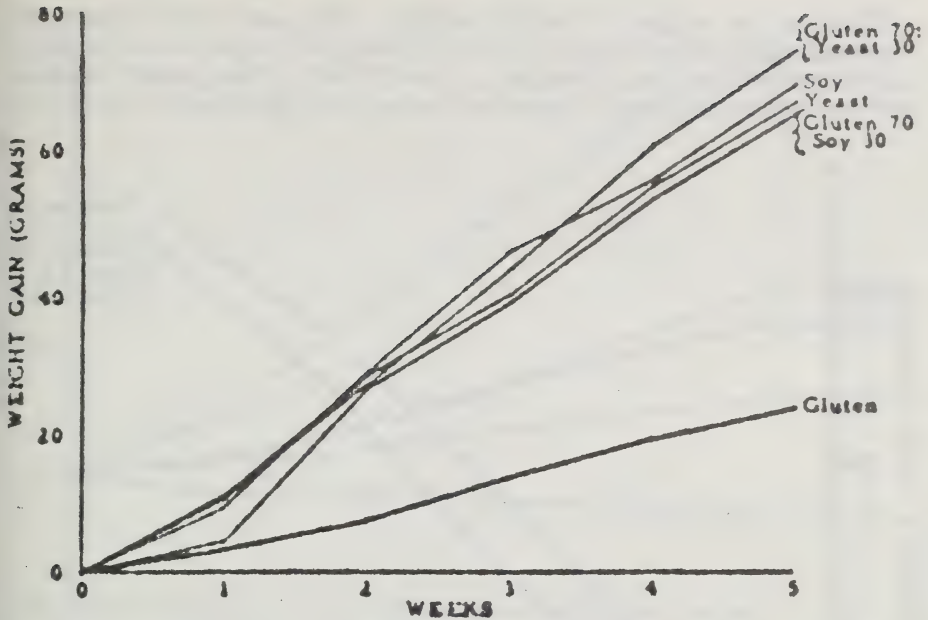


FIGURE 2.—Supplementary effect of yeast and soy proteins upon wheat gluten protein. Seventy percent of the total protein in the diet is supplied by wheat gluten; the remaining 30 percent of the protein is supplied either by brewers yeast or soy protein. All other essentials have been supplied to the diet.

amino acids are required by man. These are called essential, or indispensable, amino acids. This does not mean that the other amino acids are not important or essential, but simply that they can be synthesized by the body from available amino acids in sufficient amounts to meet the body's requirements, if the protein diet is adequate in other respects. In discussing protein needs, biochemists are today primarily interested in the amino acids in the diet rather than in a specific protein. Thus protein nutrition has evolved into amino-acid nutrition.

In the past, great emphasis has been placed upon eating complete proteins; that is, those that contain all the indispensable amino acids. It was for this reason that such foods as meat, milk, and eggs were given the designation "perfect" proteins. Accordingly, emphasis was placed upon the consumption of these protein foods to the exclusion of others. This, of course, led many to feel that the protein part of their diet should consist largely of animal proteins. Now investigators are describing as rather antiquated the idea that a person should seek to obtain his protein from what are often described as "complete," or "perfect," proteins. In ordinary diets, even of the pure vegetarian type, the protein part of the diet consists, not of one protein, but of many, hence the chance that any of the essential amino acids will be missing from the diet, is highly improbable.

What is the origin of the old concept that one should secure his protein largely from animal sources because such proteins are perfect," and why such a radical change in views? Most of the pioneer work in protein evaluation was in terms of measuring the growth of rats on

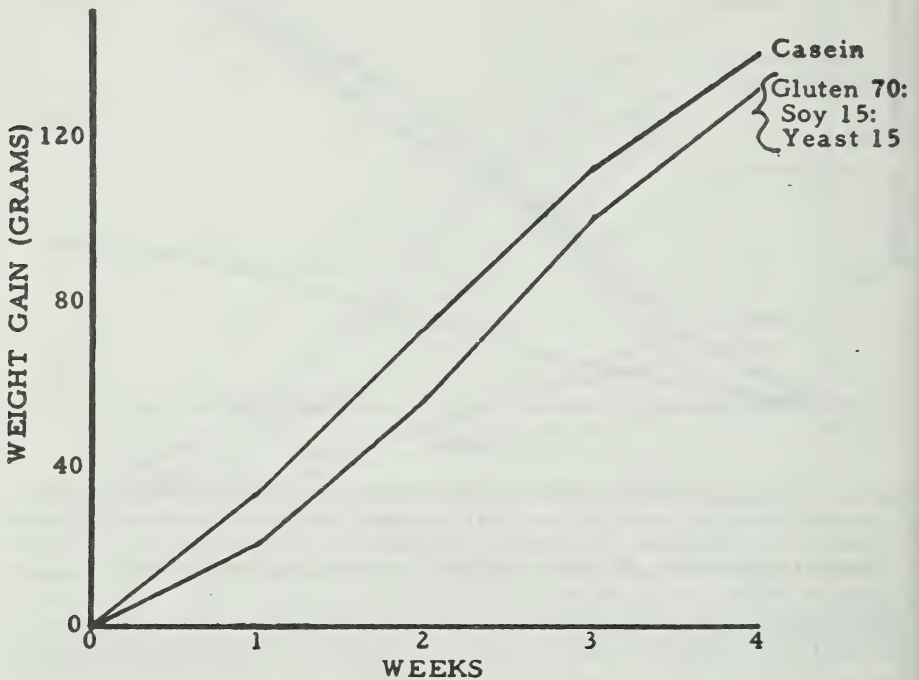


FIGURE 3.—Growth response of gluten-yeast-soy protein combination compared with milk casein. Both diets have 18 percent total protein; 70 percent of the total protein in the combination is from wheat gluten, 15 percent from soy protein, and the remaining 15 percent from brewers yeast. All other constituents of the diets are adequate for normal growth of the albino rat.

single protein sources. Since meat, milk, and eggs gave rapid maximum growth, these were declared to contain superior proteins, while other foods were said to contain inferior proteins. However, the idea of evaluating proteins on growth alone is changing. We now know that experimental animals fed proteins in such quantity and quality as to produce very rapidly growth develop more degenerative diseases and die at an earlier age than those fed a diet to produce an adequate, though slower, growth.

We also know today that a food should not be labeled inferior because its proteins do not contain adequate amounts of the essential amino acids. As already stated, we eat a number of proteins at each meal, and they so supplement one another that a protein combination of good quality is assured. Hence the question of a "perfect" protein is irrelevant. What is more, no one would think of living on one food. Such a diet would become extremely monotonous. God has given us a variety to enjoy.

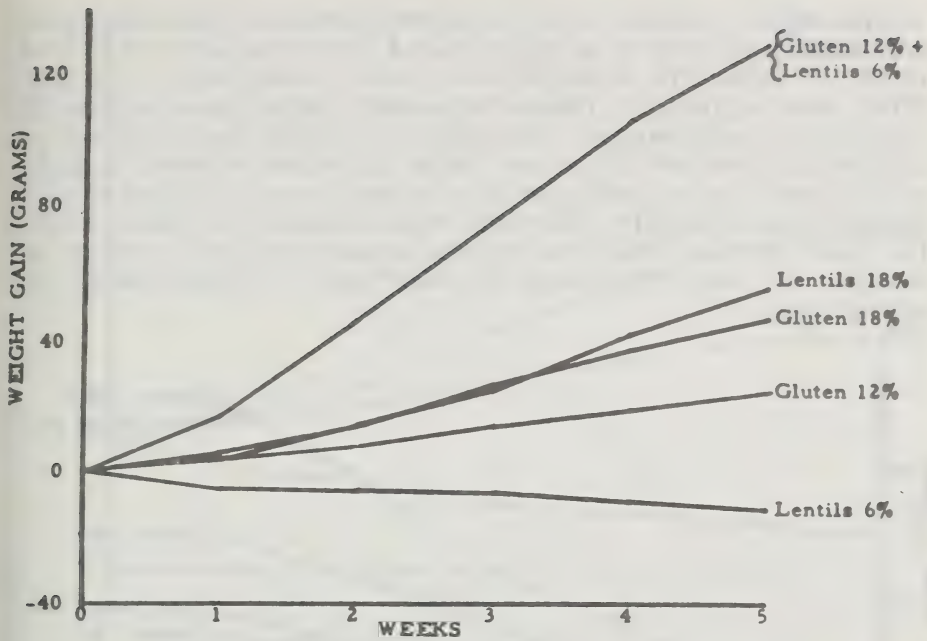


FIGURE 4.—Supplementary relation of wheat gluten and lentil proteins. The protein content of each diet is indicated. The combination of the two proteins in one diet provides a diet containing 18 percent protein. All other dietary essentials are supplied in adequate amounts.

When we speak of one protein supplementing another we mean that when two or more proteins are fed together the quality of the combined proteins is higher than that of either protein alone. For example, proteins of grains are low in the essential amino acid lysine, but have an adequate supply of sulfur amino acids, methionine and cystine. On the other hand, legumes are relatively deficient in sulfur amino acids. Thus the grains supplement the legumes and vice versa, with the result that a person eating grains and legumes secures a protein supply of excellent quality.

The idea that meat is essential in the diet is not founded upon controlled experiments. Many outstanding investigators agree that meat is not essential in the diet and much might be gained by dispensing with it. Dr. E. V. McCollum at Johns Hopkins has stated that a vegetarian diet, supplemented with fairly liberal amounts of milk, is the most healthful diet for man (H. S. Diehl, "Textbook of Healthful Living" [1945], p. 147). Dr. Fredrick J. Stare of Harvard has well observed: "Lumberjacks may demand plenty of red meat, but that demand rests on habit and not on nutritional or medical basis."—*Am. J. Pub. Health* 33:1444, 1943.

It is a rather common occurrence to see a patient in poor nutritional state because of being on a highly refined diet or consuming a limited variety of foods. The doctor says the patient needs meat in the diet. When meat is given, the patient improves; thus a false conclusion is reached that meat supplies something in the diet that could not be supplied by a variety of natural foods. Experiments reveal that the patient would have shown the same improvement if he had simply changed from his highly refined diet to one consisting of natural foods. The meat provided additional needed amounts of such nutrients as vitamins and minerals, which are also found in abundance in the natural foods.

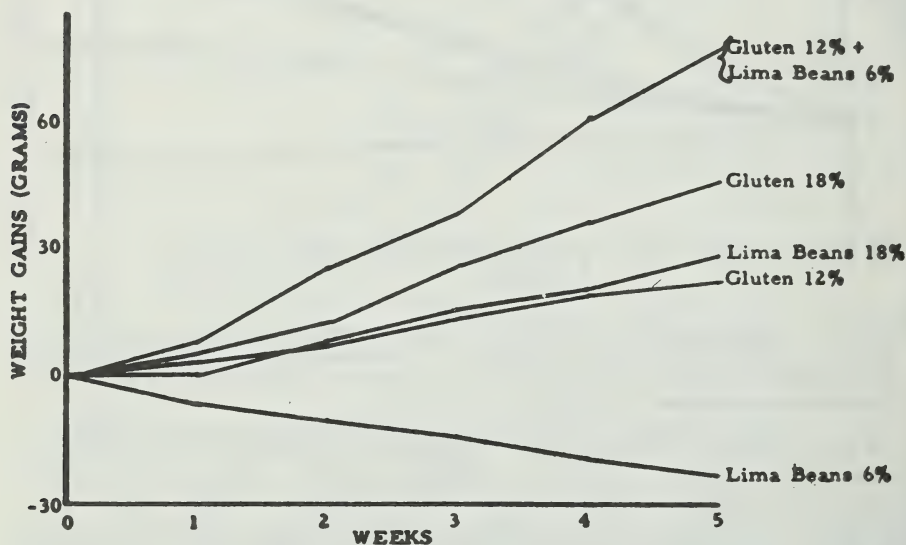


FIGURE 5.—Supplementary relation of gluten with limabean protein.

Whether from custom or blind experiment, those rural peoples throughout the world who have subsisted primarily on plant foods have selected food combinations, such as legumes and grains, that possess a strikingly high nutritive value. The combination of peas or beans with bread provides a protein of comparable quality to that of meat as a "main dish." "In any mixed diet, even if wholly of plant origin, the proteins are sure to be sufficiently varied to compensate for any individual inadequacies in amino-acid content, if only the total amount of protein is sufficient."—WRIGHT, *Applied Physiology* (1952), p. 1055.

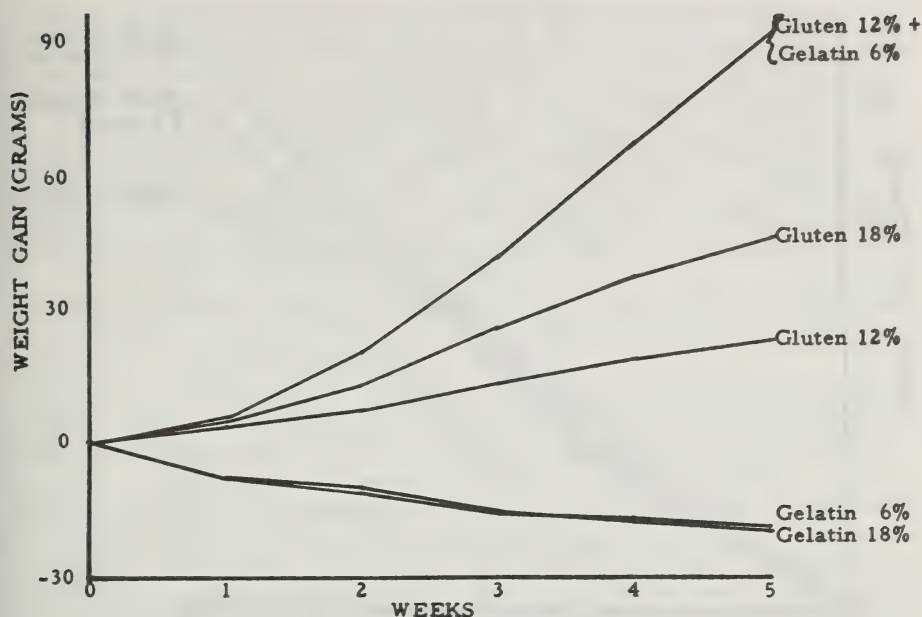


FIGURE 6.—Supplementary relation of gluten with gelatin.

The question is sometimes asked: What is the value of commercially prepared vegetable protein foods? Are they essential in the diet? In the light of the facts just given, the obvious answer is that no one food is essential in the diet. However, these particular foods, when combined with other foods in the usual pattern of diet, will both complement and supplement the other food proteins and supply a protein mixture of high biological value. At the same time the basic dietary pattern is not significantly altered. The following statement from the authoritative work, "The Chemistry and Technology of Food and Food Products" (1951), provides general information as to the value of these foods in the diet: "In recent years there has been considerable interest in the production of 'meat' substitutes in which wheat gluten containing 60 to 80 percent protein has been used. * * * If properly formulated, they are highly nutritious."—Volume 1, p. 218.

To provide further information in this area, an intensive study is in progress at the College of Medical Evangelists on the value of these vegetable protein foods in different food combinations. The accompanying graphs represent only a portion of the results of this study. The research thus far has been in terms of relative growth on experimental rats. Studies, employing other factors, are in progress.

Since an 18 percent casein (protein of milk) diet has been used as a standard in the rat studies, several food proteins were incorporated into otherwise complete diets at an 18 percent level, so that the protein is the only altered or limiting constituent. The results are shown in figure 1. The varied growth responses are due principally to differences in amino-acid composition of the proteins.

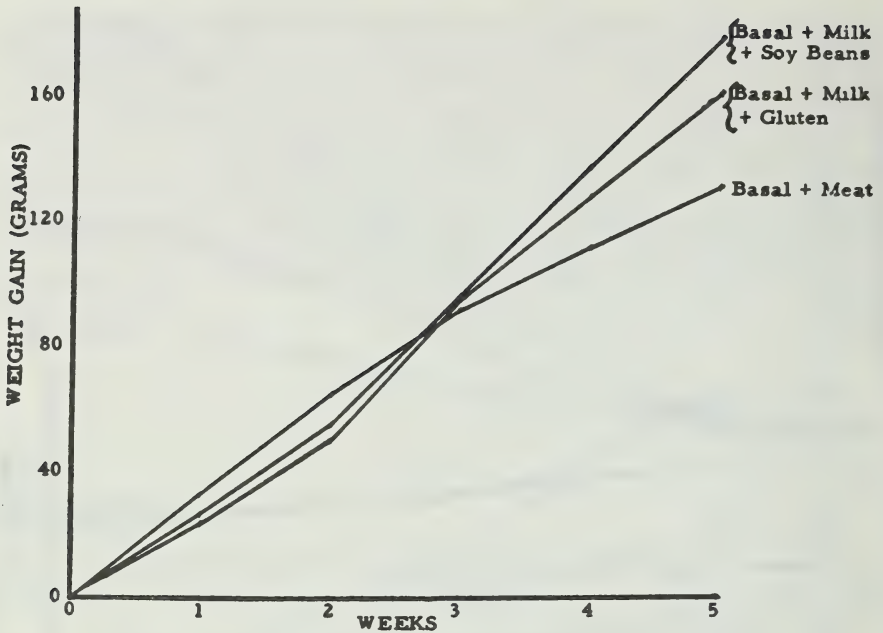


FIGURE 7.—The effect of adding meats, gluten with milk, or soybeans with milk to a mixed diet containing no entrees. The mixed diet is a multiple of several meals collected from the College of Medical Evangelists cafeteria. This diet without entrees is the basal ration.

Since wheat gluten is widely used as a part of entree dishes, a study of its effect in diets was undertaken. Gluten is known to be low in the amino acid lysine. In the present work, gluten with added lysine supported growth equal to that of the soybean protein. Studies in infants have shown that gluten plus lysine is comparable to an evaporated milk diet (*J. Nutrition* 38:222, 1949). Gluten is also low in B vitamins, which one would expect to obtain in protein foods. Thus protein foods high in lysine and B vitamins, such as soybeans, garbanzos, lentils, beans or peas, milk, eggs, yeast, wheat germ and others, would be expected to supplement wheat protein.

As shown in figure 2, when 70 percent of the protein in the diet is from gluten and 30 percent from soybean or yeast, the combinations are comparable to the yeast or soybean diets when fed at the same protein level. In these experiments all essential nutrients were added so that protein was the only altered or limiting factor.

In figure 3 the protein combination of gluten 70, yeast 15, and soy 15 gives growth equal to casein of milk. The yeast-soy portion can be varied to 20-10, 5-25, or any other combination, and still show similar supplementary action.

The remarkable supplementary action of lentils and gluten is demonstrated by figure 4. The combination gives more than twice the growth response of either lentils or gluten fed at a protein level of 18 percent.

Studies of gluten fed with other foods in the same proportions as in the lentils experiment have shown that the growth response of the animals was essentially the same when the diets contained milk, eggs, garbanzos, soy, wheat germ, lentils, or cashews. Results thus indicate that proteins of these foods have the same supplementary value when added to wheat gluten. Note that proteins even in a single food (wheat germ and gluten) supplement one another. As already seen in figure 1, there is a vast differences in the growth response of animals on milk diet as compared with lentil diet alone, but lentils are as good as milk when supplemented with gluten protein.

Although peanuts, peas, or lima beans and gluten did not produce as good growth as the above foods with gluten, yet some supplementary action was seen in each study (Fig. 5).

Figure 6 reveals that rats dependent for their protein on the animal protein, gelatin, lost weight, but when gelatin was supplemented with gluten, excellent growth resulted. Thus it is possible for an animal protein to be supplemented to advantage by a plant protein.

These are only a few examples of studies that have been conducted and are not necessarily designed to be a pattern of diet to be followed. These studies show that if so many combination of only two protein sources show supplementary action, how much more would the wide variety of protein sources ordinarily eaten each day supplement one another. On the basis of these studies and many others, it becomes important to reform the traditional habit of speaking of animal protein as if it alone were efficient in supplementary action, for we now know that many plant proteins are similarly effective. Therefore, when the sources of proteins in the diet are fairly well diversified, there is little danger of the protein's being inadequate from the qualitative standpoint.

To show these supplementary relationships in a mixed diet, several meals were collected from the cafeteria of the College of Medical Evangelists. These meals, without the entree, or main protein dish, were mixed thoroughly and called the basal ration. To a portion of this basal ration was added a variety of meats as normally consumed by the average American. To a second portion was added wheat gluten with milk, and to a third portion soybeans with milk. The meats, wheat gluten, and soybeans were added in such quantities to provide equal amounts of protein. These three diets were then fed to three groups of rats. Figure 7 shows that the animals on diets with milk and soy beans, or gluten, grew as well as those on the meat diet.

To study the adequacy of a lacto-ovo-vegetarian (milk-eggs-vegetarian) diet, a week's diet was collected from the Loma Linda Hospital. The entrees were removed, as above, from a portion of the diet and replaced by a mixture of meats containing the same quantity of protein as the entrees. The meat diet was compared with the regular hospital diet in animal experiments. Figure 8 shows that the lacto-ovo-vegetarian diet was as good as the meat diet in protein quality.

These studies indicate that meat is not needed in order to obtain a diet of high protein quality. This experimentally observed fact simply confirms what the eminent nutritional authority Dr. H. C. Sherman of Columbia University declared some years ago: "When grain products, vegetables, fruits and milk have all been given their full places in the diet, the result is a food supply and dietary of such excellence

that the extent to which meats, fats, and sweets are added is of relatively little consequence in normal nutrition.”—“*Essentials of Nutrition*” (1951), p. 334.

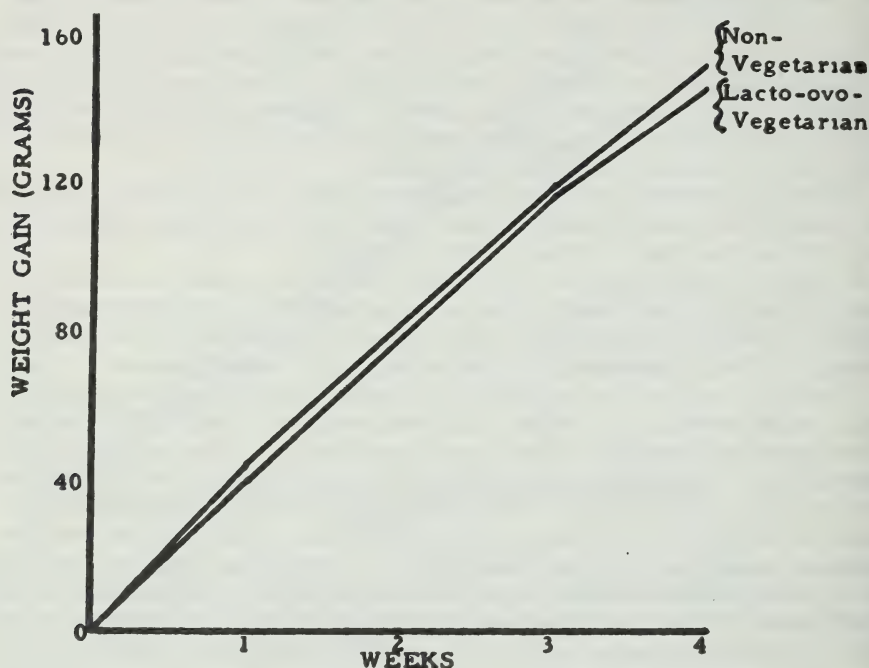


FIGURE 8.—Growth response of rats on a lacto-ovo-vegetarian diet and non-vegetarian diet. The vegetarian diet is a week's diet as served to patients at the Loma Linda Hospital. The nonvegetarian diet is the same except that the vegetarian entrees were replaced by a mixture of meats containing an equal amount of protein.

In another study, a complete menu from a pure vegetarian diet—that is a vegetarian diet that excludes milk and eggs—was collected over a one-week period at the La Sierra College cafeteria. The entrees were collected separately and are designated “entree” in figure 9. The remaining portion of the diet was finely ground, mixed thoroughly, and used as the basal ration. When indicated, milk or soy milk was added in an amount to provide one glass per meal. Five different rations were prepared: (1) the basal ration, meat, and milk; (2) basal, entree, and milk; (3) basal, entree, and soy milk; (4) basal, wheat gluten, and milk; and (5) basal and meat. These were fed to five groups of rats with seven rats in each group. All diets produced excellent growth, thus demonstrating an excellent quality of protein, whether from a pure vegetarian, lacto-vegetarian, or a nonvegetarian diet. It is interesting to note that similar growth is obtained when gluten is the entree in the lacto-vegetarian diet.

Many studies have shown that the quality and quantity of protein of a pure vegetarian or lacto-vegetarian diet is more than adequate to meet the protein needs in normal nutrition (*The J. Clin. Nutrition* 2:73, 1954). However, there is one point of caution that should be given to those who might contemplate adopting a pure vegetarian diet for a period of several years. Although a lacto-vegetarian diet pro-

vides adequate amounts of vitamin B_{12} , no presently known practical source of this vitamin is present in plant foods. A small percentage of pure vegetarians—those using neither milk nor eggs—in England and Holland have developed a vitamin B_{12} deficiency after three or four years on this type of diet; however, some did not show a deficiency even after ten years on a pure vegetarian diet.

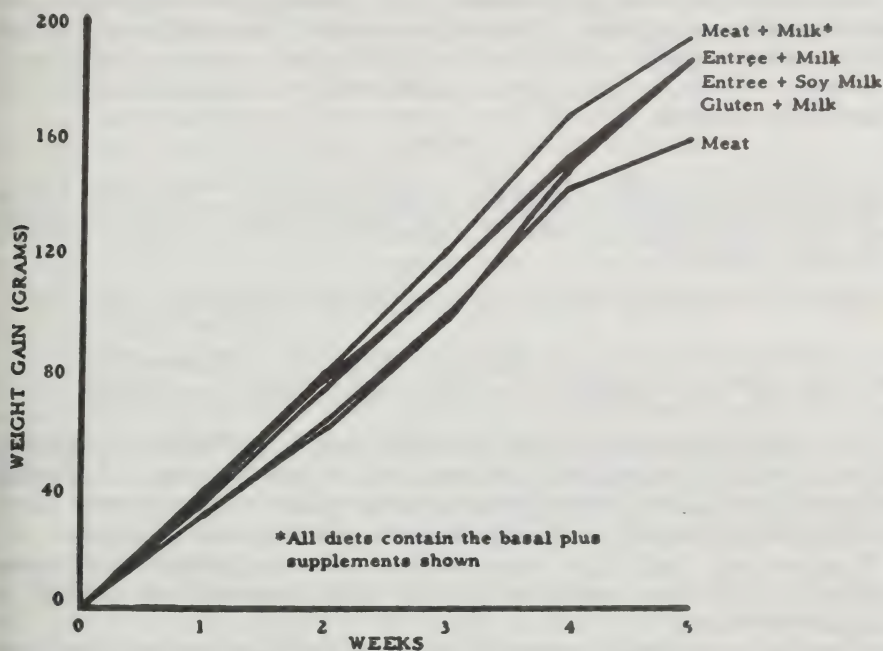


FIGURE 9.—Growth response of rats on various cafeteria diets. Food from a week's menu of a pure vegetarian diet—that is, a vegetarian diet that excludes milk and eggs—was collected from the La Sierra College cafeteria. The vegetable protein entrees were collected separately and are designated "entree" in the graph. The vegetarian diet without the entree is called the "basal." Where indicated, milk or soy milk was added in an amount to provide one glass per meal. The following rations were mixed and fed to separate groups of rats. (1) Basal+meat+milk, (2) Basal+entree+milk, (3) Basal+entree+soy milk, (4) Basal+wheat gluten+milk, (5) Basal+meat.

Many Eastern people subsist on a pure or almost pure vegetarian diet, but they usually use soy sauce (made with molds) or other foods treated with molds that produce adequate quantities of this vitamin for their needs, whereas the Western peoples did not adopt this custom when eating a pure vegetarian diet, thus the deficiency seen. However, much more study needs to be given to this problem before any definite conclusion can be reached.

"The time will come when we may have to discard some of the articles of diet we now use, such as milk and cream and eggs; but my message is that you must not bring yourself to a time of trouble beforehand, and thus afflict yourself with death. Wait till the Lord prepares the way before you."—"Counsels on Diet and Foods", p. 206, compare pp. 208, 210. These counsels have been given concerning the possible danger of dispensing with milk in the diet, not because of the

protein factor, but probably because of the lack of vitamin B₁₂ in plant foods, which could be supplied by an average daily intake of one glass of milk or soybean milk containing vitamin B₁₂.

To sum up the matter: today it can be scientifically demonstrated that the lacto-vegetarian diet is wholly adequate. In the light of this, the counsel given to us long ago takes on new force and value: "Fruits, grains, and vegetables, prepared in a simple way, free from spice and grease of all kinds, make, with milk or cream, the most healthful diet. They impart nourishment to the body, and give a power of endurance and vigor of intellect that are not produced by a stimulating diet."—Counsels in Health, p. 115.

THE PHYSIO-CHEMICAL ANSWER TO THE QUESTION "WHY DO THOSE WHO CONSUME MEAT AND FATS DIE PREMATURELY DUE TO ISCHEMIC HEART DISEASE?"

(By W. P. Neufeld, M.D., Burnaby, British Columbia, Canada)

What follows is the result of 40 years of observation, study and investigation into cause and prevention.

By way of introduction, let me state that I am William Neufeld, M.D., a general practitioner of medicine in the Province of British Columbia, Canada. I still engage in active practice, though my interest is more and more becoming focused on the question above.

I am setting forth facts, observations and conclusions which have evolved as the direct result of dealing with thousands of patients in the past 40 years.

I urge any reader to continue with me for the next few minutes, for the problem of ischemic heart disease is of great importance. You have my thanks for your careful attention.

The common complaint by patients of indigestion led me into my life's study. I had not been long in practice—about 1936 I believe—when I realized that most of my patient's problems were related to food, and of course, because of the functional nature of the difficulties, X-ray studies were generally of little help.

I began to study the medical literature on this topic and to visit numerous medical universities where studies were being undertaken, for instance, the Mayo Clinic, the University of Minnesota, and other centres in Cleveland, Toronto, Chicago, St. Louis, New York, New Orleans and Berlin, Germany.

Now, after years of applying these physiological principles on my patients, I am currently engaged in writing a book which will, in a large measure, document my experience and studies. In the book I stress the importance of food to general health, but, perhaps more importantly, the unquestionable importance of food as a cause of ischemic heart disease and coronary thrombosis.

What follows is a brief summary of my findings and beliefs in the matter of food and our health, food and life, and food and death. In all the years of my practice, I have never once had reason to doubt these principles of the particular physiology to which I subscribe.

Although the food we eat affects every cell in a human body, in the determination of health and efficiency, I shall confine my remarks

mainly to the effect which the wrong kind of food can have on the heart.

In our Western society, the most common cause of death given by doctors is heart failure. Heart failure is the given cause of more deaths than cancer and diabetes combined. I am positive that many of my distinguished readers are familiar with the dread toll in your country. But, would it hurt to ponder, for a moment, the stark fact recorded by the eminent Dr. A. C. Guyton in his recent medical physiology text. Dr. Guyton points out that 35 percent of the annual deaths in the United States are due to heart failure.

That astounding statistic surely must provoke serious thought by medical scientists—and serious action by governments.

The question so often asked is—why does the heart deteriorate? And that question leads to another—why do so many people die when they are so young? Neither question has been answered adequately because, primarily in our Western society, we are not facing up to the consequences of logic and common sense. I apply that last thought in the broadest possible sense.

The structure and metabolic chemistry of the heart as a unit is relatively simple. The heart is a pump. It consists of strong muscles, valves and an intricate nerve mechanism. The heart gets its blood supply through the coronary arteries, and, if these arteries are not damaged by outside factors, they can, as they normally do, profuse the heart muscles with oxygen and nutrient-laden blood. So we see that the cause of death can never be the heart itself. We must look further and ask questions.

The factors that damage the heart are outside the heart itself. I have often thought that, figuratively speaking, the heart has been saying to medical researchers for thousands of years—"keep my environment unpolluted and I will continue to pump health and energy for many more years."

The liver is responsible for the condition of the blood that profuses the coronary arteries. This organ, therefore, creates a pure or polluted environment for the heart. A troubled, unhealthy or damaged liver simply cannot perform properly. Therefore, if we do not care for our liver, we are asking for heart trouble.

Let me now be simple and direct:

There is usually only one way we can damage the liver. That is by consuming food which is bad for our system. Unfortunately, out of sheer ignorance (or contrived ignorance), millions of North Americans insult their lives every day and prolonged abuse of this kind usually results in a funeral.

Can I persuade you to use the utmost concentration during the next few minutes?

You will realize that the liver is the largest organ of the body and that its function is to purify our blood every minute of every hour of our lives. Try to think of the liver—this huge mass tucked under the diaphragm—as the filter organ of your body. The question then arises: What happens to a filter when it is all clogged up?

As stated, the liver is tucked under the diaphragm with the heart located above the liver. One understands more about the liver by the following "body geography." The liver divides the body into halves.

The head, neck, chest and arms are located above the liver and the abdomen and legs, of course, are below. Because of this position, the liver has a commanding, controlling, governing power over the blood circulation and it is this power which is so often not realized.

The return flow of the blood from the abdominal organs and legs has to flow through the liver into the heart. The blood is carried through the liver by two large veins. One carries the blood which is laden with molecular products of digested food from the stomach and intestines. In the liver, this vein is dispersed in small, microscopic branches which wind between the liver cells to deposit the food. As they leave the liver, these small branches are gathered into a large vein as it enters the heart. We will be referring back to this very important anatomical relationship.

The vein from the legs is the largest in the body and does not divide into branches as it passes through the liver into the heart. When we are "all right," the blood returns easily from abdomen and legs through the liver into the heart and we feel comfortable and well.

However, the difficulty can arise, and often does, when one eats food to which the liver is allergic. As is common in other allergies (such as nasal and skin) the liver cells swell. That is, they become enlarged with fluid. The small microscopic veins we mentioned previously (the ones winding between the liver cells) become strangulated as the liver cells swell. Thus the flow of blood is blocked to a very great degree. The blood still moves, but very slowly.

The heart keeps on pumping the blood into the abdominal organs, while the return flow is slowed down by the swollen liver. In other words, the heart puts out blood, but gets less return flow. Dr. J. T. Barrett in his textbook "Immunology, 1974" (page 255) states that in an extreme anaphylactic (or allergic) reaction, the swollen liver can hold back 60 percent of the circulating blood volume. This is very hard on the heart and it can be either severely damaged or cardiac arrest might occur. This often happens during sleep.

Food grown in gardens and cereals in fields rarely will cause an allergic reaction by the liver. Neither will dairy products and eggs. Even if, on occasion, there is a sensitivity to fresh fruit, this can be overcome by cooking.

However, it is altogether different with meat. It has been confirmed by many research documentations that animal protein causes the most devastating, often fatal, liver reactions. Almost daily I see cases where denatured meat has caused a major allergic reaction.

We are all familiar with denatured meat, but we are not so familiar with the danger of denatured meat. Cooked meat stored in a refrigerator will change color. That is the result of oxidation. If that denatured meat is eaten by a person whose liver rejects the deteriorating food, he or she can become violently ill, quite possibly requiring an ambulance to hospital. I advise my patients to be extremely cautious about hamburger, meat loaf, sausages and weiners. It is obvious that some meats of this kind in our marketplaces might not be as fresh as we would like.

Let me now outline other factors which I consider, on the basis of my practical experience, to be destructive to the body—particularly the heart and brain.

Careless chronic eating, with the resultant repeated allergic reactions by the liver, will, as common sense dictates, causes damage to the liver cells. If damaged, the liver loses the ability to control the blood cholesterol. As the pancreas controls the blood sugar level, so is the liver intended to control the vital blood cholesterol level.

Most North Americans over the age of 50 fear, to some extent, the hardening of the arteries, but few realize it is linked to a malfunctioning liver. When the liver, damaged by careless eating, loses its cholesterol control, the cholesterol rises to abnormally high levels and it is this excess cholesterol which causes, in turn, the hardening and narrowing of the arteries.

Now, we are getting closer to heart failure deaths. (Or so-called heart failure death). It is my contention that most of our heart failure deaths are the result of a malfunction or malfunctions outside the heart. In some cases, there is nothing organically wrong with a dead person's heart even though he suffered cardiac arrest.

With the narrowing and hardening of the arteries supplying the heart muscle, we also have a similar occurrence in the arteries of the brain. This in turn leads to a premature deterioration of the whole body, and the continual possibility of an acute myocardial infarction or a stroke.

When the liver is swollen in an allergic reaction, thus blocking the return flow of blood to the heart, the heart can suffer severe damage, as stated earlier, or it can stop, because of hypoxia, or lack of oxygen. There is another effect of liver allergy and that is a tendency to increased blood clotting. Thus we can have either a blood clot in the brain or in the heart.

All this from eating denatured meat?

My answer is yes.

Cooked meat undergoes a chemical change, even if stored in a refrigerator, and can cause severe allergic reactions. Myocardial infarction, cardiac arrest, or severe damage and subsequent invalidism can result.

In clinic experience these incidents usually occur at night, during sleep.

Dr. Charles K. Friedberg of Los Angeles, author of the modern book "Diseases of the Heart" cites the statistics of 1,108 cases of acute coronary thrombosis:

52 percent occurred during sleep or rest.

48 percent occurred during routine activity, such as walking.

Only two percent occurred during unusual activity or exertion.

I have often consoled relatives who, only a few hours earlier, had shared a feast with a man now dead. Invariably he has been a meat eater. Invariably, he has been one who scoffed at advice to reduce his meat intake.

In my many years of practice, I have seen many habitual meat eaters in difficulty and, sadly, I have seen many in death. I have never seen a meat-abstainer, or a vegetarian suffer a massive allergic reaction of the liver with disastrous heart or brain complications.

This is not to say that vegetarians do not suffer liver allergy reactions. But such reactions caused by the odd fruit or the odd vegetable to which an individual's liver system may be allergic is mild compared to those reactions which are caused to a habitual meat eater.

I urge my patients to use milk, cheese and a moderate number of eggs. Cereals have proven to my satisfaction to be well tolerated. Veg-

etables of course. Nuts can be added as a good source of protein and I rather prefer nuts to eggs if the cholesterol level is anywhere near the danger level.

Such a diet will enable the liver to function to the best of its natural purpose. The arterial walls of the heart and the brain will remain flexible and soft—capable of prolonging our activity and our lives. In this regard, surely it is time that a detailed examination be made of the diet of certain of the peoples of Southeast Europe, where an age of 120 is not unheard of.

In my last few words to you of the U.S. Senate Select Committee on Nutrition and Human Needs, let me say that all the medical evidence I have seen confirms, to my satisfaction, that a vegeteraian diet prevents ischemic heart disease. I have seen statistics and I am sure you have statistics available to you, which offer overwhelming proof to persons who respect logic and common sense.

WAKE FOREST UNIVERSITY,
BOWMAN GRAY SCHOOL OF MEDICINE,
DEPARTMENT OF PATHOLOGY,
Winston-Salem, N.C., July 27, 1977.

Senator GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs,
U.S Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: Thank you for asking if I had any comments on "Dietary Goals for the United States". Unfortunately, my schedule kept me from replying in time to meet your May 29 deadline. I do, however, have serious doubts about the wisdom of setting forth the recommendations given for general public consumption. I realize that to wait for the final word is to invite paralysis of action, and perhaps an abdication of what you and the rest of the committee see as your public duty. However, as a medical scientist my doubts are of sufficient magnitude to say "wait a while".

For the most part, my reservations are those voiced to your committee by Dr. Ahrens. He was kinder about the Oslo survey than I would have been. Facts are not established by polls or committees, but by experiment, thus the Oslo survey means nothing to me as a scientist. It is an index of what those people polled thought at the time, thus has some interest from that point of view. One matter which concerns me, and has for years, is the one of what harm might come from following the "Dietary Goals . . .". For example, there is evidence that increasing the intake of unsaturated fat may lead to gallstone formation, and even to accelerated aging and increased incidence of cancer. This concern was not sufficiently looked into, in my opinion.

Like Dr. Ahrens, I would suggest that additional research be done before "Dietary Goals" is given general circulation. The matter is so complex that to do otherwise might lead our descendants to rue the day it was issued, if indeed it was the start of a national diet change as recommended.

Thank you again for inviting comment.

Sincerely,

ROBERT W. PRICHARD, M.D.,
Professor and Chairman.

VANDERBILT UNIVERSITY,
SCHOOL OF MEDICINE,
DEPARTMENT OF BIOCHEMISTRY,
Nashville, Tenn., August 12, 1977.

Senator GEORGE MCGOVERN,
U.S. Senate,
Washington, D.C.

DEAR SIR: I write to ask you to lead your Select Committee on Nutrition and Human Needs in a reconsideration and retraction of the "Dietary Goals for the U.S.," released last Spring. Those goals arose from incomplete and prejudiced information. They are neither practical, sound nor persuasive for the citizenry. The goals reflect the biased interests of selfish scientists and segments of the food industry which hood-winked your staff. It is distressing to contemplate the damage done both to the image of science and to the public's welfare. Here, in brief, are summarized the main points of my objections to your published goals:

1. There is no substantial evidence to support the hypothesis that dietary changes will influence the behavior of the epidemic forms of cardiovascular disease. That advice is a promotion of self-interested industries and the irrevocably committed group of scientists who subsist on the financial support of that hypothesis. Enormously expensive trials of the diet-heart hypothesis have failed to confirm it.

2. Attempts to manipulate the proportion of carbohydrate in the U.S. diet have no proof of efficacy for either obesity or diabetes. Those diseases result from sloth and gluttony not from a particular nutrient mixture. They will not be influenced by manipulating the proportion of carbohydrate in the diet.

3. The level of fat in the diet has not been related causally to any disease and in particular, not to either obesity or to cancer. Those who contend this are adventurists.

4. The amount of saturated fat in the diet has not been shown causal for any disease. A large probability exists that the hydrogenated fats created during the industrial process are damaging to health because of their content of the unnatural "trans" isomers. I for one do not permit such adulterated fats as Fleischmans Margarine and hydrogenated cooking fats in my house for that reason. The low-fat, polyunsaturated diets recommended by Stamler et al. are well-known to double the incidence of gall bladder disease and in two of five long-term studies they increased the incidence of cancer. These facts emphasize that the dietary modifications recommended are not harmless.

5. Dietary cholesterol is a small and inconsequential part of the total body supply. Egg consumption is not related to cholesteremia—and eggs are a nutritious food—considerably better than "Egg Beaters."

6. It is dietetic foolishness to tell people to eat 3 gm or less salt per day while allowing the food technologists to add salt at will.

7. The most menacing factor in the U.S. nutritional scene today is the health damage caused by alcohol, and yet your document does not address that problem.

The release of this document presents a nutritional debacle. Listening to only part of the story, your staff has prepared a report which has betrayed you as a fair and intelligent Senator. The damage results

from the mistaken belief by the general public that these goals reflect the best informed and most expert scientific opinion when they do represent the vociferous fringe of selfish industrialists and the self-interested scientists. Unless you can manage to change them, the "Dietary Goals for the U.S." will go down with swine flu, laetrile and the other "fraudulent" treatments.

You can take steps to correct this debacle at least in part. I hope that you will.

Sincerely yours,

GEORGE V. MANN, M.D.,
Associate Professor of Biochemistry.

CORNELL UNIVERSITY,
DIVISION OF NUTRITIONAL SCIENCES,
Ithaca, N.Y., September 7, 1977

Sen. GEORGE MCGOVERN,
Dirksen Senate Office Building,
Washington, D.C.

DEAR SENATOR GEORGE MCGOVERN: I should like to congratulate you and your colleagues with your fine efforts to establish "Dietary Goals for the United States." With minor exceptions I endorse them wholeheartedly. I have also studied the testimonies by Drs. R. Olson and E. H. Ahrens Jr. and the statement by the National Dairy Council all of which express opposition to the proclamation of these dietary goals.

Although from a purely scientific point of view one can argue about the strength of the evidence supporting the recommendations for dietary changes, it seems plausible to me that our Government should act upon the considerable amount of knowledge that we now have. In addition to the documentation provided to your committee, it is my personal belief that the connection between dietary cholesterol and fat, and the causation of heart disease is greatly strengthened by the numerous studies on experimental animals. I make this statement as someone who has engaged in this type of study for about 30 years, and who has published close to 200 scientific articles on the subject.

I hope that your committee will continue its good efforts, not only in implementing current nutrition knowledge to improve our nation's health, but also in providing funds for scientific research in all health-related areas.

Sincerely,

DONALD B. ZILVERSMIT, Ph. D.,
Professor, Nutritional Biochemistry.

THE ALBANY MEDICAL COLLEGE OF UNION UNIVERSITY,
Albany, N.Y., August 25, 1977.

Sen. GEORGE MCGOVERN,
Select Committee on Nutrition and Human Needs,
Washington, D.C.

DEAR SENATOR MCGOVERN: I think it was a courageous step to recommend dietary goals to the American public. We all recognize that more research is necessary to clarify these controversial issues, but I

endorse the position of the Select Committee, that it is reasonable to suggest prudent guidelines.

Personally, I think it would be appropriate to publicize these goals by a series of major television programs, in which the data for each recommendation is presented and the unresolved or conflicting facts are pointed out.

I regret that a leading nutritional body, the A.M.A. Department of Foods and Nutrition, has decided to oppose the adoption of your recommendations.

Sincerely,

LYN HOWARD, M.D.,
Director, Clinical Nutrition Program.

AMERICAN MEDICAL ASSOCIATION,
Chicago, Ill., April 18, 1977.

HON. GEORGE MCGOVERN,
*Chairman, Select Committee on Nutrition and Human Needs, U.S.
Senate, Washington, D.C.*

DEAR SENATOR MCGOVERN: Enclosed for consideration by the Senate Select Committee on Nutrition and Human Needs is the statement of the American Medical Association in response to the publication entitled "Dietary Goals for the United States."

We would appreciate the inclusion of our comments in the record.

Very truly yours,

JAMES H. SAMMONS, M.D.,
Executive Vice President.

C. STATEMENT OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association is pleased to present its comments on the publication entitled "Dietary Goals for the United States" as prepared by the staff of the Senate Select Committee on Nutrition and Human Needs.

At the outset we wish to commend the efforts seeking to achieve an increased level of health among our citizens. Diet of an individual can vitally affect his health status. However, it must be recognized that diets must not be standardized nor be inflexible for all persons but must reflect individual needs.

We believe that it would be inappropriate at this time to adopt the proposed national dietary goals as set forth in the Report on Dietary Goals for the United States. The evidence for assuming that benefits to be derived from the adoption of such university dietary goals as set forth in the Report is not conclusive and there is a potential for harmful effects from a radical long term dietary change as would occur through adoption of the proposed national goals. A discussion of our concerns with the Report follows:

BACKGROUND

The Report on Dietary Goals consists of several introductory statements as to the desirability of establishing six national "dietary goals" as part of a national health policy; an explanation of the goals and their rationale; and five recommendations to Congress to encourage achievement of the dietary goals.

The purpose of the Report, as expressed in the Foreword of the Report, is (1) to "point out that the eating patterns of this country represent as critical a public health concern as any now before us"; (2) to provide practical guides to the individual consumer as well as to set national dietary goals "to reduce health costs and maximize the

quality of life"; and (3) "to serve as a catalyst for government and industry action to facilitate the achievement of the recommended dietary goals."

In addition, the Foreword states that: "Action is needed to determine how changes can be made regarding the content of nutritional information provided to the public; the kinds of foods produced; how foods are processed and advertised; and the selection of foods offered by eating establishments. Our national health depends on how well and how quickly Government and industry respond."

Statement of dietary goals

The Report sets forth six dietary goals for the United States. These goals are as follows:

(1) Increase carbohydrate consumption to account for 55 percent to 60 percent of energy (caloric) intake.

(2) Reduce over-all fat consumption from approximately 40 percent to 30 percent of energy intake.

(3) Reduce saturated fat consumption to account for about 10 percent of total energy intake; and balance that with poly-unsaturated and monounsaturated fats, which should account for about 10 percent of energy intake each.

(4) Reduce cholesterol consumption to about 300 mg/day.

(5) Reduce sugar consumption by about 40 percent to account for about 15 percent total energy intake.

(6) Reduce salt consumption by 50 percent to 85 percent to approximately 3 gm/day.

Recommendations for Government action

The Report also presents five recommendations for government action to encourage the achievement of the foregoing dietary goals. These recommendations are:

(1) That Congress provide funds for a public education program in nutrition based upon the above or similar goals and including nutrition education in the classrooms, in the federally funded food assistance programs, for school food service workers, and by the Extension Service of the Department of Agriculture.

(2) That Congress require food labelling for all foods containing the following information: percent and type of fats, percent sugar, milligrams of cholesterol, milligrams of salt, caloric content, a complete listing of food additives for all foods, and the nutrition labelling which is currently voluntary.

(3) That Congress provide funds for the conduct of studies, and pilot projects that would develop new techniques in food processing and institutional and home meal preparation aimed at reducing "risk factors" in the diet.

(4) That Congress increase funds for human nutrition research and that Congress establish a Committee for the coordination of human nutrition research undertaken by the Departments of Agriculture and HEW.

(5) That the Departments of Agriculture and HEW form a joint committee to periodically consider the "implications of nutritional health concerns on agricultural policy."

COMMENTS

The AMA is concerned about the assumptions made in the report relating to the benefits assertedly to be derived by adoption of a major change in our national dietary practices along the lines stated in the study. We discuss these concerns below.

In addition, we believe that the dietary goals asset forth in this Report should not be adopted at this time nor should the recommendations to implement these goals be adopted. For reasons which we point out, we believe that insufficient evidence exists at this time to support the need for or the benefit from major changes in the national diet as proposed.

General

The Report's major premise is found in an introductory statement to the report:

"... our diets have changed radically within the last 50 years, with great and often very harmful effects on our health. These dietary changes represent as great a threat to public health as smoking. Too much fat, too much sugar or salt, can be and are linked directly to heart disease, cancer, obesity, and stroke, among other killer diseases. In all, six of the ten leading causes of death in the United States have been linked to our diet."

The Report suggests that the incidence of heart disease, cancer, hypertension, diabetes, obesity and tooth decay could be reduced by making qualitative and quantitative changes in "the American diet." The goals are laudable; however, the American Medical Association believes that there are insufficient data to recommend such changes in the diet on a nationwide scale. This is not to imply that certain dietary practices of many Americans should not be improved.

For example, evidence that links the American diet with the American death rate from ischemic heart disease is suggestive, fragmentary, and even conflicting. The epidemiological data showing associations between diet and cancer of the colon and breast cancer are very tenuous. While epidemiological observations suggest a relation between salt ingestion and hypertension, they fail to support the hypothesis that salt consumption is a major factor in causing hypertension in persons in the United States.¹ Diabetes is a multifactorial disease; its precise etiology has not been established and there are no primary studies that establish any specific dietary factors as diabetogenic. Moreover, patients with diabetes require diets tailored to the individual.

Heart disease

One of the diseases that the Report suggests could be affected through adoption of the dietary goals is heart disease. The strongest evidence for an association between diet and any one of the ten leading causes of death in the United States is that of diet and coronary heart disease. However, in 1969, Dr. Theodore Cooper, Director of the National Heart Institute, National Institutes of Health, stated: "Evidence which is suggestive, fragmentary, and even conflicting links the American diet

¹ American Academy of Pediatrics, Committee on Nutrition: Salt intake and eating patterns of infants and children in relation to blood pressure. *Pediatrics*, 53:115-121, 1974.

with the American death rate from ischemic heart disease."² This statement is still valid in 1977.

Coronary heart disease is a multifactorial condition. Many risk factors have been identified, but these are not all of equivalent importance in population groups or in individual patients, and the evidence for harm done by their presence ranges from strong to weak or only suggestive. Generally those considered to be of greatest importance have been age, sex, hypertension, hyperlipemia (especially an elevated serum cholesterol level), diabetes, and cigarette smoking.³

Dietary studies on the incidence of heart disease generally have been limited to attempts at reduction of serum cholesterol levels and have been successful in lowering the serum value 10 to 20 percent. Those studies published up to 1969, which form the basis for dietary advice issued by various health groups, were reviewed by Cornfield and Mitchell,⁴ who pointed out the difficulty in evaluating the data because of variability in design of the studies and considerable range in the magnitude of results. They also indicated that principles must be observed in future studies if more definitive knowledge is to be obtained on the question of whether lowering serum lipid levels will reduce the risk of coronary heart disease.

In a Report of the Diet-Heart Review Panel of the National Heart Institute,² the Panel examined all the evidence on the proposition that the incidence of coronary heart disease might be reduced through dietary measures. The Panel stated that the evidence was "most suggestive but not convincing." It was the Panel's opinion that the important points at issue remain unproven. It is not proven that dietary modifications can prevent atherosclerotic heart disease in man. It is not known that the demonstration of such a proof could or would find general applicability in our society. Also, it is not known what constraints and responses would arise in the course of applying such knowledge in the population. Moreover, answers to these important questions in the Panel's view can only come from definitive field trials to test the scientific hypothesis that the relationship between serum cholesterol levels and coronary heart disease incidence is a causal relationship rather than an indirect association.

The Panel concluded, among other things:

(1) In the absence of conclusive proof on the Diet-Heart question any dietary advice to the American public will always lack authenticity and authority, will be conducive to half-measures and will meet opposition which cannot be effectively countered.

(2) ... should the result [definitive field trials] indicate that a change in the national diet will be required, this would have considerable impact on the economy of the country; it was concluded that with appropriate planning, the food industry would be able to make the necessary adjustments.

² Mass Field Trials of the Diet-Heart Question: Their Significance, Timeliness, Feasibility and Applicability. Report of the Diet-Heart Review Panel of the National Heart Institute, New York, N.Y., American Heart Association Monograph No. 28, 1969.

³ Paul O.: The Multiple Risk Factor Intervention Trial (MRFIT): A National Study of Primary Prevention of Coronary Heart Disease. *Journal of the American Medical Association*, 235:825-827, 1976.

⁴ Cornfield J., Mitchell S.: Selected risk factors in coronary disease: possible intervention effects. *Archives of Environmental Health* 19:382-394, 1969.

(3) Unless definitive trials are instituted now, one of two equally undesirable situations will result; either, scientifically sound advice to the American public will be delayed and many lives that might be saved will be lost; or, the public will react with apathy to dietary advice based on inconclusive evidence and any beneficial results of such a program will not be identifiable.

A national study of primary prevention of coronary heart disease, the Multiple Risk Factor Intervention Trial, has been undertaken by the National Heart and Lung Institute.³

The American Medical Association concurs with the opinions and judgments expressed by the Panel and does not believe it is appropriate to recommend radical dietary measures to the population as a whole until completion and assessment of results of studies currently underway.

Cancer

Another disease category which would allegedly be influenced by adoption of the dietary goals as set out in the Report is cancer. The Report suggests a link between dietary fat and cancer of the breast and colon and between consumption of fiber and the existence of bowel cancer. While epidemiological data show a correlation between high fat intake and cancer of the colon, the case against high fat intake is weak because there are populations that have a high fat intake but little bowel cancer.⁵ Any conclusion that diet is related to cancer of the colon and any specific tests of dietary hypotheses must first await demonstration of dietary differences between patients with colon cancer and persons free of the disease, i.e., case-control studies.⁶

Furthermore, high fat intake has not been identified as a risk factor in breast cancer.⁷

As to dietary fibers, there is no scientific consensus on the definition of dietary fibers or how to measure them. Fiber is a general term applied to several different food components that vary in their chemical and physical characteristics. It is not yet possible to define whether or not fiber deficiency or excess in the diet exists or can constitute a protective or noxious element in the diet.⁸

Hypertension

Another alleged benefit from adoption of the dietary goals is, in the view of the Report, a favorable change in the incidence of hypertension by setting a goal of consumption of salt at 3 grams daily.

Difficulties arise in attempting to recommend a suitable range for dietary salt because of the tremendous range of biological tolerance in normal human beings, the widely different levels of salt appetite, and the cultural significance which salt has in relation to food.⁹

⁵ Berg JW: Diet, in Fraumeni JF, Jr. (ed): "Persons at High Risk of Cancer: An Approach to Cancer Etiology and Control," New York, New York, Academic Press, 1975, p. 201.

⁶ Berg JW, Howell MA, Silverman SJ: Dietary hypotheses and diet-related research in the etiology of colon cancer. *Health Services Reports* 88:915-924, 1973.

⁷ Berg JW: Can nutrition explain the pattern of international epidemiology of hormone-dependent cancers? *Cancer Research*, 35:3345-3360, 1975.

⁸ Mendeloff AI: Dietary fiber. *Nutrition Reviews*, 33:321-326, 1975.

⁹ Denton D: Instinct, appetites and medicine. *Australian, New Zealand Journal of Medicine*, 2:203, 1972.

The effects of salt consumption on health have been well stated by the Committee on Nutrition of the American Academy of Pediatrics¹ in the following:

"Because of the prevalence of essential hypertension in adults, there is a major public health concern with its causes . . . These factors include race, family history, stress, variations in endocrine and kidney function, and body habitus. Salt has also been cited as causing hypertension. There is no question that an increase in salt intake by most hypertensive patients will increase their blood pressure. The converse also is true. The question is whether salt intake induces hypertension and, in particular, whether salt consumption by the general population in this country is a risk.

" . . . epidemiological observations suggest a relation between salt ingestion and hypertension but fail to support the hypothesis that salt consumption is a major factor in causing hypertension in persons in the United States.

"Approximately 20 percent of children in this country are at risk of developing hypertension as adults. The factors that will induce hypertension are genetic, which cannot be modified, and environmental, which can be modified. . . .

"The role of salt intake as an environmental factor in the induction of hypertension has still to be defined. For 80 percent of the population in this country, present salt intake has not been demonstrated to be harmful, i.e., hypertension has not developed . . .

"Salt appetite for some is an important expression of personal preference in relation to diet; for others, salt-containing foods have important cultural values. Present evidence does not provide a firm basis for advising a change in the dietary salt intake for the general population. There is a reasonable possibility that a low salt intake begun early in life may protect, to some extent, persons at risk from developing hypertension."

Organizations such as the American Heart Association and the American National Red Cross, professional and allied professional health care personnel, pharmaceutical companies, and civic groups have been actively involved in mass screening programs to detect elevated blood pressure¹⁰ and thus to bring about proper treatment.

Furthermore, most patients with hypertension can be effectively treated, their blood pressure lowered, and their risk of death and adverse effects reduced. Medical management for some patients may include sodium restriction or calorie restriction or both.

Therefore, we believe that the recommendation of the Report to set salt consumption as a national dietary goal is inappropriate.

Diabetes

Diabetes is another disease that the Report suggests would be affected by adoption of the dietary goals. Indirect studies of the relationship between diet and the development of primary diabetes mellitus cannot provide a definitive answer but over-eating has been implicated as a factor associated with a rising incidence of maturity-onset diabetes, especially when combined with under-activity and obesity. The few direct studies that have been done support the hypothesis.¹¹ It is likely that avoidance of overeating and obesity would prevent the appearance of adult-onset diabetes in genetically-prone individuals.

The primary emphasis in the dietary management of the individual diabetic patient is weight control through appropriate calorie reduc-

¹⁰ Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure: A Cooperative Study. Journal of the American Medical Association, 237:255-261, 1977.

¹¹ Davidson S, Passmore R, Brock JF, Truswell AS: Diabetes Mellitus. Human Nutrition and Dietetics, 6th ed., Edinburgh, London, Churchill Livingstone, 1975, pp. 412-436.

tion rather than the proportion of carbohydrates and fat in the diet as the Report suggests. Diets to control diabetes (or other conditions) must be tailored to meet individual needs rather than seeking a uniform diet for all.

Obesity

Obesity is another condition addressed by the Report. Obesity is a major public health problem in the United States. It has been associated with four different types of hazards to health—changes in various normal body functions, increased risk of developing certain diseases, detrimental effects of established diseases, and adverse psychological reactions.

Although the effect of weight reduction in the prevention of disease is not clearly known, there are many diseases in which significant, obvious benefits are attained with the loss of coexisting excess weight. Obesity aggravates cardiovascular disease and osteoarthritis and increases the liability to hypertension, atherosclerosis, hernia, and gallbladder disease.¹² Also susceptibility to diabetes mellitus may be enhanced by obesity combined with inactivity.

Therefore, the prevention or treatment of obesity would be more effective in modifying the course of diabetes, hypertension, and one of the risk factors of coronary heart disease than any other diet modification aimed at reducing the incidence of specific diseases.

However, the main dietary determinant of obesity is total amount of calories (energy) in the diet and not their source (i.e., whether or not the calories are provided by carbohydrates, fat or protein). In practice, the choice of food and the eating patterns of overweight individuals are as varied as those people who are of normal weight or who are underweight. Those suffering from obesity should seek individual medical advice and, where appropriate, follow a prescribed individual diet. Adoption of national dietary goals is not an answer to obesity and could prove detrimental if followed by individuals properly requiring medical supervision for their particular condition.

CONCLUSION

The evidence for benefits to be derived from the adoption of the dietary goals as set forth in this Report is insufficient and the potential for harm for the radical long term dietary change in "the American diet" is unknown. Further, the genetic and cultural heterogeneity of the population in the country would, no doubt, resist a rigid policy with respect to dietary goals. While the goals set forth in this Report would appear to be laudable in many respects, the American Medical Association believes that at this time it would not be appropriate to adopt such dietary goals.

The dietary goals of the Report concerning modification in the amount and type of fat and cholesterol and the restriction of salt intake to no more than 3 grams daily are comparable in many respects to therapeutic diets. Such diets must be formulated to meet the individual needs with appropriate medical dietary counselling on an

¹² Burton BT: Obesity and leanness. Human Nutrition, 3d ed., McGraw-Hill Book Co., 1976, pp. 229-247.

individual basis. Strict adherence is required to obtain the desired results.

The American Medical Association does not consider it appropriate for the government to adopt national goals that specify such matters as the amount and proportions of total fat, type of fat, sugar, cholesterol, or salt content in the diets of the general public as these national goals advocate.

Rather, we believe that individual programs to prevent or to treat obesity through decreased caloric intake along with programs aimed at improving physical fitness would be the most effective means of improving the health of our American citizens.

As to the recommendations stated in the Report, we believe that they should not be adopted in implementation of the national goals. As stated, the recommendations would encourage the Federal government to undertake a massive, nationwide educational program to gain public acceptance and incorporation of the dietary goals as personal goals. Furthermore, the recommendations carry with them the underlying potential for prohibiting the sale or for discouraging the agricultural production of certain food products which may not in the view of the government be supportive of the dietary goals.

In conclusion, we urge that the Report not be adopted.

CHAPTER III

TRADE ASSOCIATION COMMENTS

SALT INSTITUTE,
Alexandria, Va., July 11, 1977.

HON. GEORGE MCGOVERN,
Chairman, Senate Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: We wish to thank your staff for taking the time to hear our concerns about the suggested dietary goal for salt and for agreeing to consider our position.

We believe that the goal to reduce salt consumption may very well work against the committee's aim of getting people to eat good diets of nutritious foods, since it may leave those foods less palatable and, therefore, less acceptable. Salting is a personal choice for taste, which, in the end, is the final determining factor whether one accepts certain foods.

It is our opinion, supported by the vast majority of the medical profession, specifically, the American Medical Association, the American Heart Association and the American Academy of Pediatrics, that a reduction in daily salt intake is not an important or even significant dietary goal for the general public.

The level at which daily salt intake would be considered excessive for the general population is controversial, but there is no evidence that the current average per capita intake of 5 to 10 grams per day is too much. Before there can be a conclusion on how much or how little one should have, particularly in any national dietary goal, more research would certainly be needed. Even researchers who think there may be a link between high salt intake and hypertension refer to levels much higher than 5 to 10 grams in attempting to show a connection.

Three grams per day is an arbitrary figure that has no scientific basis. For persons who must definitely be on low-sodium diets that would be no help, since it probably would be too high. For everyone else, 3 grams per day could, at certain times of physical stress and hot temperatures, be too low.

We further feel that if the committee decides, after careful review of our statement and those of the AMA and AHA and the view of the AAP, to include reference to salt in the dietary goals, it would be more practical to suggest that Americans try to exercise reasonable prudence in salt consumption.

That recommendation may very well receive wider acceptance from the scientific community and the general public than the specific salt reduction goal the committee has recommended.

Again, we appreciate the opportunity to present the views of our industry, both in formal comments and in the personal meeting with the committee staff.

Sincerely,

WILLIAM E. DICKINSON, *President.*

Enclosure.

STATEMENT OF THE SALT INSTITUTE—RE: "DIETARY GOALS FOR THE UNITED STATES"

The Salt Institute is a trade association that represents the interests of the world's major salt producers. It is concerned with all salt uses, including the nutritional value of salt as a food, and with criticism of salt.

Salt is essential to life, so much so, that the body has a built-in regulator—the kidneys—to remove excess salt or to retain salt if the amount in the body is deficient. It is a scientifically supported fact that too little salt can have a serious effect on the human body and, in some cases, loss of too much salt could even be fatal.

The role of sodium in hypertension has been the subject of debate for many years. Positions in the medical profession range from little or no concern for the role of sodium intake to suggestions that high sodium intake may be a cause of hypertension.

The Federal Trade Commission, in a complaint ¹ against advertising for a salt product with reduced sodium content, has this to say:

In truth and in fact, while some medical authorities have suggested that there is data which apparently supports such a representation, it has not been established that there is a causal connection between sodium intake and high blood pressure or water retention, or that a reduction in the level of sodium intake will promote or maintain good health.

The continuing 28-year Framingham Heart Study ² has this to say on the subject: "A crude assessment of dietary salt intake in Framingham revealed no relation between salt intake and blood pressure."

To quote further:

No relationship of blood pressure level to the salt intake rating on dietary interview could be demonstrated. The subjects were divided into four groups on the basis of sodium excretion (expressed as grams of sodium chloride). There was no evidence that the blood pressure of these subjects was related to their 24-hour sodium output.

Of the environmental factors examined, including physical activity, tobacco smoking, salt intake, other nutrient intake, mineral content of water, alcohol consumption and educational status, only alcohol consumption and educational status had some noticeable effect. Those in higher educational brackets appeared to have slightly lower blood pressure and men with high levels of alcohol intake had slightly higher blood pressures.

Among other factors, relative weight had the greatest effect on blood pressure level. A summary of the study contained in a brochure

¹ Federal Trade Commission File No. 742 3258, "Agreement Containing Consent Order to Cease and Desist in the Matter of Morton-Norwich Products, Inc. and Needham, Harper & Steers Advertising, Inc."

² "Hypertensive Cardiovascular Disease: The Framingham Study" by William B. Kannel, M.D., and Thomas R. Dawber, M.D. as reprinted from "Hypertension: Mechanisms and Management."

prepared by the Heart Information Center of the National Heart Institute does not even mention salt.

The Primary Drinking Water Standards³ established by the United States Environmental Protection Agency set no standards for sodium. On the matter of sodium, those standards state:

For a healthy individual, the intake of sodium is discretionary and is influenced by food selection and seasoning. The intake of sodium may average 6 grams per day without adverse health effects. (Six grams of sodium is equivalent to 15 grams of salt).

It's interesting to note that in a publication "Recipes for Fat Controlled Low Cholesterol Meals,"⁴ published by the American Heart Association, most of the recipes call for addition of salt, from "to taste" to 1½ teaspoons. This would indicate that it is the opinion of AHA nutritionists that the intake of sodium is not of vital concern.

Let's look closer at the two opposite positions on the relationship of salt and hypertension.

One position is expressed in the June 14, 1975 edition of "The Lancet,"⁵ a British medical journal:

Current practice allows no place for salt restriction in the management of hypertension. The doctor who tells his hypertensive patient with normal renal function to avoid salt is wrong on two grounds. Firstly, the reduction in salt intake with such advice falls far short of that required to produce a significant effect upon blood pressure. Secondly, existing drugs are potent enough to render the misery of effective lifelong salt restriction unnecessary.

The article further states that patients with advanced renal failure and clear evidence of sodium retention, that is, those on dialysis or approaching dialysis, require sodium restriction, but it points out they are extremely rare in non-specialist clinical practice.

The opposite position claims a connection between high sodium intake and hypertension. We emphasize "high" because a recent study by Dr. Lot Page⁶ supporting that position refers to 15 to 20 grams of sodium per day, equivalent to 50 grams of salt. Daily consumption of salt in the United States is estimated at 5 to 10 grams. That's 2 to 4 grams of sodium. The high intake of 15 to 20 grams of sodium does not tie in with the Committee's goal of reducing intake of salt to about 3 grams per day, equivalent to 1.2 grams of sodium. Since the average intake of salt is only 5 to 10 grams, nowhere near the "high" category, it seems illogical to attempt to reduce such a level that has no hazard relationship.

Setting an arbitrarily low standard for salt intake would be similar to banning use of penicillin because a very few people are allergic to it and it has caused deaths in rare instances. There are alternatives for those who are allergic, just as there are alternatives for those in the minority in the population who are required by their physicians to remain on a low-sodium diet.

Determining how much sodium a low-sodium diet patient should receive is the responsibility of that patient's physician and no one else.

³ Environmental Protection Agency "Primary Drinking Water Standards, 1972."

⁴ "Recipes for Fat Controlled Low Cholesterol Meals" published by the American Heart Association, 7320 Greenville Avenue, Dallas, Texas 75231.

⁵ "The Lancet," June 14, 1975 page 1325.

⁶ "Epidemiologic evidence on the etiology of human hypertension and its possible prevention" by Dr. Lot B. Page, Newton and Boston, Massachusetts, published in the American Heart Journal, April 1976, Vol. 91, No. 4, pp. 527-534.

The American Heart Association won't even give the average person who requests it a copy of any of its restricted sodium diets without a doctor's prescription. That's how serious that organization considers setting daily dietary sodium standards. Determining where the patient gets his daily sodium and how much is a decision he must make in concert with his doctor. And in that respect, there are alternatives open to him and adjustments that can be made without setting a national salt consumption standard.

There have been estimates that 21 million persons, less than 11 percent of the U.S. population, may have high blood pressure and should be on a sodium-restricted diet. However, the American Heart Association, in a letter⁷ to a leading nutritionist, says it has no idea of the source of the statement and that it "has made no such statement and is not likely to."

The AHA says that "with the advent of effective sodium-eliminating diuretics, the need for strongly-restricted sodium diets has been sharply modified." The AHA's medical director adds that there continues to be a place for sodium-restricted diets in patients with congestive heart failure and uncontrollable hypertension.

It would appear, then, that when we consider only congestive heart failure and uncontrollable hypertension patients among all those who may have hypertension, the total number is only a fraction of 21 million persons.

Anything affecting such a small portion of the public is hardly a candidate for a national dietary goal, particularly when there has been no proved causal connection between sodium and hypertension. Focusing on such an insignificant item as salt limitation in the diet can only dilute efforts to provide the public with reasonable dietary information.

The American Medical Association, which represents thousands of physicians, has challenged the position that diet has a connection with heart disease and other diseases as well. The AMA statement to this committee mentioned that there are too many other risk factors more important than diet.

"While epidemiological observations suggest a relation between salt ingestion and hypertension, they fail to support the hypothesis that salt consumption is a major factor in causing hypertension in persons in the United States," the AMA statement says.

Referring to the Dietary Goals report alleging a favorable change in the incidence of hypertension by setting a goal of consumption of salt at 3 grams daily, the AMA says,

Difficulties arise in attempting to recommend a suitable range for dietary salt because of the tremendous range of biological tolerance in normal human beings, the widely different levels of salt appetite and the cultural significance which salt has in relation to food.

The Committee on Nutrition of the American Academy of Pediatrics,⁸ speaking on the effects of salt consumption on health, says,

The role of salt intake as an environmental factor in the induction of hypertension has still to be defined. For 80 percent of the population in this country, present salt intake has not been demonstrated to be harmful, i.e., hypertension has not developed. . . .

⁷ Letter from Campbell Moses, M.D., Medical Director, American Heart Association to Dr. Olaf Mickelsen, Professor of Nutrition, Michigan State University, August 25, 1972.

⁸ American Academy of Pediatrics, Committee on Nutrition: Salt intake and eating patterns of infants and children in relation to blood pressure. *Pediatrics*, 53:115-121, 1974.

Salt appetite for some is an important expression of personal preference in relation to diet; for others, salt-containing foods have important cultural values. Present evidence does not provide a firm basis for advising a change in the dietary salt intake for the general population.

The American Heart Association, through its nutrition chairman, had told the Committee its claims about the effect of salt in the diet cannot be substantiated scientifically.

We commend the Senate Select Committee on Nutrition and Human Needs for its concern over nutrition. However, we note that the Committee and its staff obviously have been very selective in their source of references about the effect of salt on health. They apparently chose to rely almost entirely on George Meneely, M.D. and Harold Battarbee, Ph D.,⁹ whose work has largely been based on studies of the relationship of high sodium and low potassium diets.

Those researchers continue to stress excessive consumption of salt coupled with low potassium intake. Even they state:

When an entire population eats excessively of salt, hypertension will develop among those genetically susceptible, but epidemiologic studies of salt versus blood pressure will not show a relation of salt to hypertension.

Their work has numerous references to the many studies indicating no correlation between salt intake and hypertension. They dismiss this as saying that most such studies neglect to note that where low blood pressure is found in a population consuming large amounts of salt, they were also consuming large amounts of potassium.

A normal diet that includes such foods rich in potassium as bananas, cantaloupe, grapefruit juice, tomato juice, orange juice and baked potatoes, beets, carrots, tomatoes and bran would appear to achieve the balancing effect of potassium. The very first dietary goal of the Committee is to "increase consumption of fruits and vegetables and whole grains." This goal would seem to negate the need for a goal to decrease consumption of salt, which appears to be highly questionable and have no real basis in fact. Reduction of salt would be an unpopular move at best and one difficult to obtain, based on popular taste.

Meneely and Battarbee in their paper provide a chart that shows average daily salt intake and the incidence of hypertension in different populations. Interpreting from that chart, we find that an average daily intake of salt of 10 grams would indicate an incidence of hypertension of 10 percent of the population. On that same chart, 20 percent hypertensives would indicate a daily average salt consumption of 15 grams. Using Meneely and Battarbee's chart, 5 to 10 grams, the estimated daily U.S. consumption, is not excessive for more than 90 percent of the population, so there is certainly no reason to set a salt consumption goal at 3 grams daily.

The authors admit that their recommendation of a low sodium-high potassium diet is not the current general recommendation of authoritative bodies. Current accepted practice is to use diuretic therapy "in those who require treatment" and to do no more about sodium intake than to counsel against "abuse" of salt.

"One would be naive to believe that dietary intervention would meet with success in all instances," say Meneely and Battarbee. "Were this the case, low sodium diets would already have a larger place in management of hypertension among ambulatory patients."

⁹ "High Sodium-Low Potassium Environment and Hypertension," George R. Meneely, M.D., FACC and Harold D. Battarbee, PhD, November 23, 1976, *The American Journal of Cardiology*, Vol. 38.

Drs. Paul S. Swaye and Ray W. Gifford, Jr. and J.N. Berrettoni, PhD., in their study, "Dietary Salt and Essential Hypertension,"¹⁰ conclude that family history of hypertension has a greater influence on the development of hypertension in an individual than a history of excessive salt consumption, though excessive salt consumption appears to affect adversely the severity of existing hypertension. Here again, they refer to excessive salt consumption.

The weight of evidence indicates that present sodium intake is not a major problem in hypertension or other cardio vascular diseases. Most authoritative bodies agree that reducing salt intake is not a necessity except in extreme cases where the patient is under careful doctor's control.

When such prestigious organizations as the American Medical Association, the American Heart Association and the American Academy of Pediatrics and numerous nutritionists support the position that this Committee's "Dietary Goals" as regards salt are based on insufficient scientific evidence, then it would seem that the Committee's recommendations on salt consumption should be challenged.

Salt is a necessary part of the diet. It is also widely used as a preservative and is a popular condiment that makes essential nutritional food more acceptable from a taste standpoint.

For over fifty years salt has been the principal source of iodine, a necessary nutrient important in the prevention of goiter. In order to obtain the recommended daily allowance of iodine from iodized salt, three grams of table salt must be consumed per day. Salt added to prepared foods is not iodized. Therefore, if total salt intake (including salt in foods and table use) is restricted to 3 grams per day, as the Committee recommends, the incidence of endemic goiter can be expected to increase.

In providing dietary information to the public one must be careful that such information is based on fact, that positions that are scientifically unproved are not included.

To summarize the position of the Salt Institute, we feel that there is definitely no need for a dietary goal that calls for the reduction of salt consumption. There is no conclusive medical or scientific documentation that shows a detrimental effect of salt on the general population in amounts that are currently being consumed by the average American.

The use of salt and the amounts used are choices of the individual for taste. Use of salt makes many of the essential foods in one's diet more acceptable and in that respect may actually be aiding acceptance of a nutritionally balanced diet.

There is no scientific evidence to indicate that the present average daily consumption rate of salt—5 to 10 grams—should be changed. Setting an arbitrary low level of salt consumption as a dietary goal would mislead the public into thinking that anything above that level would be dangerous to their health.

Again, we commend the Committee for its concern about proper nutrition for Americans. But for those reasons just cited, we respectfully request that the Committee delete its recommendation for a dietary goal of reduced salt consumption.

¹⁰ "Dietary Salt and Essential Hypertension," Paul S. Swaye, M.D., Ray W. Gifford, Jr., MD, FACC., J. N. Berrettoni, PhD, Department of Hypertension and Nephrology, the Cleveland Clinic Foundation, Cleveland, Ohio and the Department of Statistics, Case Western Reserve University, Cleveland, Ohio, February 6, 1971.

SUCROSE AND HEALTH

A Brief Submitted by the International Sugar Research Foundation¹ to the Select Committee on Nutrition and Human Needs, United States Senate, Following Its Report Titled, "Dietary Goals for the United States" Dated February 1977

Preliminary

This brief addresses itself only to those portions of "Dietary Goals for the United States," which deal with sucrose. For convenience, The Select Committee on Nutrition and Human Needs of the U.S. Senate will be referred to as "The Committee," "Dietary Goals for the United States" as "The Report," and the International Sugar Research Foundation as "The Foundation."

Foreword

In "The Report," Senator McGovern states: "We must acknowledge and recognize that the public is confused about what to eat to maximize health...."

Indeed nowhere is there greater confusion than with regard to sucrose consumption and good health, and one is at a loss to explain the emotional anti-sucrose tidal wave which has swept the industrialized nations in recent years and seems echoed by "The Report."

Dr. Thomas H. Jukes, Professor of Medical Physics at the University of California, Berkeley, stated:

Today, consumer activists are united against sugar. They have so bewildered the public that many people seem to think that sugar was invented in factories, and that the sweet substance present in orange juice, pineapple juice and apples is something entirely different. Many weird diets have been concocted by the doctors who write best-selling "diet books," but these always have one thing in common: they condemn sugar. (Source: Speech, May 18, 1977.)

The Committee deserves the highest praise for its persistent efforts over many years to establish the true facts about nutrition and public health, through testimonies of the most reputed scientists and knowledgeable interested persons in general.

It is therefore most unfortunate that "The Report" presents the views of individuals who, though well intentioned, must have been strongly influenced by the prevalent anti-sucrose crusade and have only "heard" those voices which denounce sucrose.

General

We regretfully and respectfully submit that "The Report" is misleading and will compound the confusion it intends to dispel; it does not reflect the consensus of the testimonies given at the Hearings, nor the views of the world's scientific community, and its recommendations are not based on scientific evidence.

Misleading language and interpretations

The use of the word "sugar" without a clear statement as to the intended meaning, i.e., sucrose or sugars in general, will mislead and confuse the reader.

On Page 12 of "The Report," Figure 1 shows the percent of total energy intake supplied by various classes of nutrients in the current diet. One reads in the contribution of carbohydrates: 22 percent carbohydrate: and 24 percent sugar. Reference to the source of these data clearly indicates that the 24 percent is contributed by sugars, i.e., nat-

urally occurring sugars found in many foods such as milk and fruit, and contained in syrups and honey as well as refined cane and beet sugar used as such, and in food processing, with sucrose accounting for only 14 percent.

Thus dietary goal number 5: "Reduce sugar consumption by about 40 percent to account for about 15 percent of total energy intake" will be erroneously interpreted to apply to sucrose.

Interpretation of some statistics appears to have been influenced by a pre-established conclusion thus misleading the uninformed reader.

On pages 14 and 15, Figures 2 and 3, show over the period 1909-13 to 1973-76 the relative changes in the sources of food energy in civilian consumption, and point out the dangers of displacement of complex carbohydrates by sucrose. Actually in the last 50 years the per capita consumption of food energy and sucrose have remained relatively constant whereas fat has increased and complex carbohydrates have decreased. In this period the significant change is the displacement of complex carbohydrates by fat, not by sucrose. If this has been detrimental then this is the trend to be reversed—not reduction of sucrose, which as an additive to grain derived foods and preserved fruit products makes them more palatable and promotes their consumption.

Irresponsible affirmations

Purporting to express the views of experts, "The Report" indiscriminately links a group of foods to a group of diseases in a "shotgun" statement which responsible scientists would not support.

On Page 9, after pointing out that fat and sugar consumption have risen to comprise together 60 percent of total calorie intake, up from 50 percent in the early 1900's, "The Report" states:

The over-consumption of fat generally, and saturated fat in particular, as well as cholesterol, sugar, salt and alcohol have been related to six of the ten leading causes of death: heart disease, cancer, cerebrovascular disease, diabetes, arteriosclerosis and cirrhosis of the liver.

This seems to imply that each and every one of the items referred to is involved in each and every one of the six diseases; it is an incredibly loose statement, highly misleading and confusing.

Disregard of statistical information

A major recommendation of "The Report"—reduce sugar consumption by 40 percent—is based on an arbitrary gut feeling, without any factual or logical justification, that some one hundred pounds per capita per year of sucrose disappearance is too high.

It is enlightening to read in the report of the Ten State Nutrition Survey 1968-1970 carried out by the Department of Health, Education and Welfare that there is a deficiency in the mean caloric intake of the populations surveyed.

Reporting on the adolescent group, (10-16 years of age), it states:

Desserts and foods that were primarily sugar (carbonated beverages, syrups and candies) contributed approximately 10 percent of the calories and their consumption was greatest in the age group 10-16 years." Page V318. "Mean caloric intakes for both males and females in all three age groups—(10-11, 12-14, 15-16)—of the adolescent population were below or only slightly above dietary standards. (Page V85.)

The recommendation of "The Report" is intended for the general public and, as such, must relate to the greatest numbers, to the mean or

median conditions and not to extremes. Based on the Ten State survey findings, the recommendation of "The Report," to reduce sugar consumption, appears contrary to the public interest.

Disregard of testimonies

The authors seem to have disregarded the testimony of the majority of scientists in order to retain the anti-sucrose views of a very small minority.

On Page 10 of "The Report," the last paragraph states:

Based on (1) the Select Committee's July 1976 hearings on the relationships of diet to disease and its 1974 National Nutritional Policy hearings, (2) guidelines established by government and professional bodies in the United States and at least eight other nations (Appendix B), and (3) a variety of expert opinion, the following dietary goals are recommended for the United States.

We have read attentively the transcript of the hearings and submit that they offer no consensus among witnesses to support the keynote statements of "The Report" nor its goals and recommendations. In those reports mentioned under (2) available to us, nowhere have we found anything comparable to the extreme views presented in "The Report". We reproduce herewith several testimonies in support of our contention.

Testimony by Dr. Theodore Cooper, Assistant Secretary for Health, Department of Health, Education, and Welfare:

In order to accomplish this (reduce calorie intake), I think what we need consider doing is to reduce our total fat intake. . . . Fat adds a calorie substance almost twice as much—9 kilocalories per gram—as compared to sugar . . . I personally believe there is some benefit to reducing our preoccupation with sweet things. (Source: Diet Related to Killer Diseases, July 27 and 28, 1976, p. 19.)

In response to a question by Senator Schweiker regarding consumption of 126 lbs of sugar per year, Dr. Walter Mertz, Chairman, Human Nutrition Institute, USDA, testified as follows:

In my opinion, it is an unhealthy trend. However I must emphasize here that this is an opinion, and unfortunately not yet scientifically proved. (Source: Part 2. Sugar in Diet, Diabetes and Heart Diseases, April 30, May 1, 2, 1973, p. 154.)

Dr. Aharon M. Cohen, Hadassah University Hospital, Jerusalem, Israel, testified:

Although we have proved that sucrose feeding causes diabetes and its vascular complications in the experimental animal, its applicability to man may still be questionable to some investigators." (Source: Part 2. Sugar in Diet, Diabetes and Heart Disease, April 30, May 1, 2, 1973, p. 165.)

Dr. Kelly M. West, University of Oklahoma Health Sciences Center, Oklahoma, USA, testified:

Thus, there is still considerable disagreement and ignorance with respect to the effects of dietary sugars in both diabetics and those who may become diabetic." (Source: Part 6A. Appendix to Nutrition and Health, June 21, 1974, p. 2987.)

Dr. Edwin Bierman, University of Washington School of Medicine, Seattle, Washington, USA, testified:

There are obvious important gaps in our knowledge. The most important one is the lack of understanding of the causes of diabetes mellitus in man. (Source: Part 6. Nutrition and Health, p. 2523.)

Dr. Theodore Van Itallie, Columbia University, New York, USA, testified:

From the foregoing brief discussion, it is possible to conclude that our understanding of the pathogenesis of most human obesity remains incomplete. (Source: Part 2. Obesity, February 1, 2, 1977, p. 53.)

In contrast to the above statements consider the following from Senator McGovern at a Press Conference Friday, January 14, 1977, Page 1 of "The Report":

Too much fat, too much sugar or salt, can be and are linked directly to heart disease, cancer, obesity, and stroke, among other killer diseases.

Disregard of scientific consensus

The overall view of "The Report", its goals and recommendations, cannot be reconciled with the consensus of the scientific community.

Beginning on Page 43, "The Report" states its goal for sugar consumption reduction and offers extremely weak justification by referring to nutrient displacement danger, cardiovascular disease, diabetes, overweight and tooth decay. We will consider these in turn to show that the testimony at the Hearings and the consensus of scientific thinking do not provide substantiation for the proposed reduction in sugar consumption.

Danger of nutrient displacement

"The Report" states on p. 44:

The most immediate problem often cited by nutritionists is the danger in displacing complex carbohydrates which are high in micro-nutrients, with sugar, which is essentially an energy source offering little other nutritional value.

This would appear a far more theoretical than practical danger, since nutrients in the food supply have practically all increased substantially from 1909-1913 to 1973, i.e., thiamin +16 percent, riboflavin +28 percent, niacin +21 percent, vitamin B₁₂ +9 percent, vitamin C +12 percent, vitamin A +7 percent and vitamin B₆ no change. Reference: "Changes in Nutrients in the U.S. Diet Caused by Alterations in Food Intake Patterns", Berta Friend, USDA, presented May 22, 1974 at an FDA Conference. As stated by Dr. Van Itallie at The Committee hearings:

It's misleading to say that there is something bad about carbohydrate because it increases the need for a vitamin. After all exercise increases the need for certain vitamins. That doesn't mean that exercise is an 'antinutrient'. (Source: Part I Obesity and Fad Diets, April 12, 1973, p. 44.)

Referring to micronutrients, Dr. Mertz stated:

Our concern is with the consequences of a marginal deficiency, and I must say that the symptoms that we have now identified are still controversial in their consequences for long term human health. (Source: Part 2. Sugar in Diet, Diabetes and Heart Disease, April 30, May 1, 2, 1973, p. 153.)

It should be noted that sucrose is not generally eaten alone, but as an additive to nutrient-containing foods, making them more palatable; it does not displace these other foods, but rather promotes their consumption. Though often referred to as empty calories, it is really *Pure Calories With No Fat and No Cholesterol*; it is an ideal energy source as an additive to other protein and nutrient providing foods.

Diabetes

The major testimony alleging a link between sucrose consumption and diabetes was that of Dr. A. M. Cohen. Referring to his experiments on rats, Dr. Cohen stated:

It remains to be proven that the observations in the animal apply to man. (Source: Part 2. Sugar in Diet, Diabetes and Heart Disease, April 30, May 1, 2, 1973, p. 165.)

Similarly Dr. William E. Dulin, Manager, Diabetes and Atherosclerosis Research, The Upjohn Co., Kalamazoo, Michigan, USA, in response to a request to evaluate Dr. Cohen's work, testified:

I think these are very interesting studies that have been carried out and I am not sure what they mean at this stage. It could mean that what he has done with this particular modification on the environment is to select for genetic backgrounds which will exhibit diabetes at some later date, and this may hold true in those animals or situations that he has studied. However, it may be very different in another population of animals and I think this should be evaluated before one makes a general conclusion. (Source: Same report, p. 277.)

Dr. James W. Anderson, University of Kentucky Medical School, Lexington, Kentucky, USA, states:

Cohen (3,4) however, was impressed with the correlation between sucrose ingestion and the presence of diabetes in Yemenite Jews (old settlers) and interpreted his clinical studies to support the concept that sucrose ingestion led to impaired glucose tolerance in normal individuals. The data of Cohen (3), however, does not support his thesis. (Source: Part 6A. Appendix to Nutrition and Health, June 21, 1974, p. 2989.)

Referring to Dr. Cohen's conclusion following his survey on Yemenite Jews in Israel, Dr. Harry Keen, Guy's Hospital Medical School, London, England, stated:

Sucrose intake was, of course, only one of the many changes in the way of life in Israel. The immigrants were more sedentary. They ate more fat, and were exposed to a variety of other stresses, dietary and social. Again one has a range of choices to explain the increased diabetes rate. (p. 2966.)

... I think I can safely conclude that, in large population samples we find no general link between sugar intake and diabetes. (Source: Part 6A Appendix to Nutrition and Health, June 21, 1974, p. 2974.)

Referring to the views of Drs. G. D. Campbell and T. L. Cleave, and the Yemenite surveys of Professor Cohen, Professor W. P. U. Jackson states:

Nevertheless the theory that sugar itself or refined carbohydrate in general is the most important diabetogenic agent of modern times requires more than this rough circumstantial evidence before it can be generally accepted. Source: *Acta Diabetologica Latina* 7 (3) :361-401, May-June, 1970.

Dr. E. Bierman, Former Chairman of the Food and Nutrition Committee of the American Diabetes Association, testified:

... There is no evidence, however, that any single nutritional factor, including excessive consumption of sugar is a cause of diabetes." Source: Part 6. Appendix to Nutrition and Health, June 21, 1974, p. 2523.

Sugar consumption in itself is not an important factor in the diabetes rate, nor in the increasing incidence of the disease." Source: *American Journal of Medicine*, "Studies in diabetes mellitus. II. Its incidence and the factors underlying its variations", Joslin, E. P., Dublin, L. I., & Marks, H. H., 187: 433-57, 1934.

The available data do not suggest that excessive consumption of sugar and over indulgence in alcohol play a part in the aetiology of diabetes mellitus." Source: *Clinical Science*, "Diet and the incidence of diabetes mellitus", Himsworth, H. P., 2:117-48, 1935-36.

It is concluded that glucose tolerance, plasma insulin and serum lipids are not significantly altered by the substitution of sucrose for starch at levels of sucrose intake comparable to those in the Western diet." Source: *Clinical Science*, "The effects of isocaloric exchange of dietary starch and sucrose on glucose tolerance, plasma insulin and serum lipids in man", Dunnigan, M. G., *et al.*, 38:1-9, 1970.

In a few studies, an inverse relationship between sucrose consumption and diabetes has been demonstrated.

In 904 normal employees of a large pharmaceutical firm in London, little relation was found between stated sucrose intake and blood sugar measured two hours after a carbohydrate load. An unexpected, highly significant *inverse* relationship was found to exist between stated sucrose intake and various measures of obesity, including skin fold thickness. . . . In an age/sex and body weight stratified subsample . . . there was, if anything, a trend to *improving* glucose tolerance with increasing levels of reported sucrose intake . . . Other studies also fail to support the alleged diabetogenic effect of sucrose consumption either in respect of newly developing diabetes . . . or of the induction of glucose intolerance . . ." Source: Keen, H. "The incomplete story of obesity and diabetes. (In *Recent Advances in Obesity Research: I*. Edited by Alan Howard, Newman Publishing Ltd., London, 1975, 116-127.)

Dr. James W. Anderson reports:

Our studies demonstrate that the consumption of an 80% sucrose diet for up to nine weeks does not impair the glucose tolerance indeed, we observed an improvement in oral and intravenous glucose tolerance in mildly diabetic individuals. Thus, the short-term intake of increased amount of sucrose or carbohydrate improves rather than impairs the glucose tolerance of both normal and diabetic individuals." Source: Anderson, J. W. "Influence of high carbohydrate diets on glucose tolerance of normal and diabetic men. (In *Is the Risk of Becoming Diabetic Affected by Sugar Consumption?* Edited by S. S. Hillebrand, ISRF, Bethesda, 1974, 44-52.)

Numerous studies have been conducted to determine the cause or causes, of diabetes. Again, it has been found that:

Many different factors can produce diabetes or increase risk of the disease; the most important of these are obesity and genetic factors. Diabetes may also be caused or precipitated by any agent that directly impairs beta-cell function or destroys beta cells (e.g. pancreatitis) or by factors that increase peripheral resistance to insulin (e.g., acromegaly or obesity). (Source: *Nutrition Reviews*, "Prevention and therapy of diabetes mellitus." West, K. M., 33(7) : July 1975, 193-198.)

On an international scale there is a clear positive correlation between adiposity and frequency of glucose intolerance. It seems unlikely that any single dietary element is responsible for both. In particular, we and others have been unable specially to inculcate dietary sucrose as a cause of diabetes. (Source: Keen, H. *Recent Advances in Obesity Research: I, Op. cit.*)

The report of the United States National Commission on Diabetes states:

Cohen produced mild diabetes without producing obesity in one group of rats by feeding high sucrose diets. These diets, however, were much higher in sucrose (72% of calories) than those consumed by any human population. Moreover, obesity and diabetes have also been induced repeatedly in animals by increasing the dietary fat. Under these conditions, the percentages of calories as starch or as sugar were often reduced. In one experiment diabetes was induced by a diet high in protein. Experiments of this kind are often difficult to interpret because two or more variables are usually changed. For example, if fat is increased, it is usually also necessary to decrease carbohydrate or increase calories. In hamsters that were prone to diabetes, Gerritsen and Dulin reduced rates of diabetes dramatically by reducing food intake. This was a quantitative and not a qualitative change in diet. (Source: *Report of the National Commission on Diabetes to the Congress of the United States*, Vol. III, Part 1, (1), December, 1975, p. 97.)

Dental caries

According to the report, "Evaluation of the Health Aspect of Sucrose as a Food Ingredient":

Dental caries is an infectious disease involving a multifactorial etiology that, in addition to the infectious organism, includes a susceptible target and an environment conducive to the growth of the infectious agent. . . . The primary substrate for the production of both plaque and organic acids is carbohydrate although other dietary factors such as phosphate can modify this response. Several investigators have found sucrose to be the most cariogenic substance

among sugars and foods tested in animal experiments. In other studies, however, glucose, fructose and other sugars have been shown to be almost as cariogenic as sucrose when fed under controlled feeding conditions. Individuals with hereditary fructose intolerance who avoid all forms of sweets . . . have fewer dental caries than the general population. However, dental caries occur in populations who have never used sugar or any other processed foodstuff.

While the cariogenicity of sucrose appears to be well established in animal studies, the differences in feeding patterns and tooth structure between experimental animals and man is significant . . . (Source: Prepared by LSRO, FASEB for FDA, 1976, p. 11.)

The results of the Vipeholm study (as reported in the FASEB report) suggest that:

. . . as in experimental animals, sucrose is cariogenic to humans but the magnitude of this effect is a function of the amount of sucrose consumed, its form and the frequency of consumption. (Same report, p. 11.)

Also,

The recent increase in availability and consumption of presweetened cereals has raised the question of their potential cariogenicity. Several studies designed to test the effect of their consumption on dental decay have not revealed any increase in caries when compared to similar diets in which nonsweetened cereals were consumed. (Same report, p. 12.)

From epidemiological studies there is considerable evidence that primitive and developing populations, especially in rural areas, have excellent teeth, but that with westernisation of diet it is usual for the prevalence of caries to increase, sometimes rapidly. It is important to note therefore, that Dr. A. R. P. Walker, of the South America Medical Research Council, reports:

We were, however, surprised that the caries position of the urban negro high school pupils remained excellent, despite a large measure of westernisation of diet, including a relatively high total sugar intake.

Dr. Walker cautions that:

None of the information that has been given implies that level of intake of these foodstuffs is unimportant. But it is apparent that in the various contexts considered, the intake of sugar sugar-containing foodstuffs was not the critical influencing factor. (Source: *British Dental Journal*, Vol. 138, No. 12, p. 463-469, 1975.)

Finally, P. Cleaton-Jones *et al* report:

While levels of intake of sugar and sugar-containing foods are not unimportant, they are not the only cariogenic factors involved, nor necessarily those of pre-eminent importance. Accordingly, it is not correct to promise patients or even to imply that a reduction in the intake of sugar or sugar-containing foods would necessarily be followed by a marked improvement in the dental caries situation. (Source: Cleaton-Jones, P., Walker, A.R.P.; Retief, D.H., *J. of Dental Assn. of South Africa*, "What is the role of sugar (sucrose) in dental caries today?" 30, 1975, p. 637.)

Overweight

There is a small segment of the population which is obese or grossly overweight; although this is of serious consequence for those so affected, "The Report" addresses itself primarily to the large number who are 10 to 15% over normal or ideal weight. This is generally considered to be due to an excess of energy intake over energy expenditure, resulting from overeating or underexercising, or both. Although statistics are not easily available to substantiate this view, it would seem that in general adults eat very reasonable meals but lead such a sedentary life that even this modest food intake adds pounds over the years. Dr.

Jean Mayer, President, Tufts University, Medford, Massachusetts, USA, formerly Chairman, White House Conference on Food, Nutrition and Health, has carried out some very interesting experiments on rats and observations on humans which lead one to believe that the sedentary lifestyle is a more important factor in overweight than overeating. From a study using high-school girls as subjects, Dr. Mayer reports:

... relative inactivity was a more important factor than relative overeating in the development of obesity in most youngsters. A very careful examination of the dietary intake of equal groups of overweight and normal-weight girls, matched for age and height, showed that the obese students fell into two groups. One, by far the larger, consisted of girls who ate a little less than the normal-weight girls, but exercised considerably less.

The association between moderate appetite, inactivity, and fatness may start early in life. . . . We found no correlation between fatness and food intake, none between growth and intake, but a very marked correlation between physical activity and intake. Fat babies had small to moderate intakes but were very inactive. Very thin babies were very active and a number of them . . . had large food intakes. (Source: *Overweight, Causes, Cost and Control*, Prentice-Hall, Inc., Englewood Cliffs, New Jersey, USA, 1968, p. 76-77.)

Further in the same book, Dr. Mayer states:

I am convinced that inactivity is the most important factor explaining the frequency of "creeping" overweight in modern societies. Our bodies' regulations of food intake was just not designed for the highly mechanized sedentary conditions of modern life. (p. 82.)

Dr. Mayer contends food intake is related to level of exercise, but that below a certain threshold of activity the mechanism does not operate.

Dr. T. Van Itallie referring to the experiments by Dr. Mayer stated:

In the light of what we know about the relationship between the activity level and food intake, it is tempting to theorize that in the United States, as a consequence of the quantity of human physical activity replaced by the internal combustion engine, the electric motor, and other advantages of an industrialized society, such as inside bathrooms, central heating, the telephone, radio and television, Americans in increasing numbers reached and passed under the low level of activity below which, to paraphrase Mayer's dictum, no further decrease in food intake occurred. (Source: "Level of physical activity and obesity: some unanswered questions." Speech presented at ISRF/CEFS Conference, Paris, March 3, 1977.)

Based on 'The Report's' page 14, Figure 2—disclosing that per capita consumption of food energy (calories) has slightly decreased from 1910 to this day, is it not reasonable to suggest that the decrease of daily energy expenditure, i.e., physical inactivity, over this period, is the major cause of the corresponding weight increase in the average individual? Very strangely 'The Report' does not even mention lifestyle and physical inactivity.

Diets are considered ineffective for weight control because they are very seldom sustained. This 'on again', 'off again' dieting has been referred to as the 'rhythm method of girth control'! Sucrose is usually the first nutrient placed on the 'no' list, probably because a portion of the consumption comes from the sugar bowl and is more easily restricted than fat which is an integral part of so many foods. Yet fat has more calories per unit weight than sucrose, and total calories from all sources is what counts. Drs. T. S. Danowski, Sean Nolan and Thorsten Stephan, University of Pittsburgh, in a paper recorded in the Committee hearings state:

Any excess of calories, be it from food, alcohol, or inactivity, is inevitably stored as body fat. It is this excess of calories, and not the type and amount of sugars, starches, protein, or fat in foods or the calories in alcohol that results in obesity. (Source: Part 6A. Appendix to Nutrition and Health, June 21, 1974, p. 3101.)

Because most diets intended to reduce weight include restriction of refined carbohydrates, especially sugar, the view prevails that high sugar consumers are overweight. The literature, however, does not support this view.

In 1965, Papp *et al* reported studies on patients with ischaemic heart disease and control groups, principally in relation to their intake of sugar. Among other findings, no correlation was found to prevail between sugar intake and proneness to obesity. Paul *et al* reported similar studies; they reached the same conclusion. In 1971 Dalderup and van Haard published studies carried out for the Dutch National Council. They noted that no correlation appeared to prevail between sugar intake and obesity; they also concluded that no correlation was apparent with diabetes, coronary heart disease and expectation of life. At the 7th International Sugar Meeting, held in Paris, Bruggerman and Visser described extensive investigations on numerous population groups in the Netherlands; they found no correlation between sugar intake and overweight or obesity. (Source: Walker, A.R.P., *South African J. of Science*, 71, (7), 1975, p. 202.)

It has been stated that human obesity is not a single syndrome.

The regulation of body weight in man is governed by an interaction between energy intake, energy expenditure, and the efficiency of the body's biochemical mechanisms. The input of energy is accomplished through ingestion of food, and expenditure is the sum of muscular activity and the energy required by the organism to grow and to maintain its own internal state. (Source: Jordan, Henry A. and Levitz, Leonard, "Behavior Modification in the Treatment of Childhood Obesity", In *Childhood Obesity*, Edited by Myron Winick, John Wiley & Sons, New York, 1975, p. 141.)

There is also believed to be,

... a genetic component to obesity ... if neither parent is obese, there is only a 7% chance of the child's being obese. If one parent is obese, the chance is 40% whereas if both parents are obese, the chances jump to 80%. (p. 6.)

Environmental factors are also important, and as physical activity is decreased,

... the genetic potential has more and more chance of being expressed. (Source: Winick, Myron, Ed., *Childhood Obesity*, John Wiley & Sons, New York, 1975, p. 6.)

Dr. Albert J. Stunkard, General Hospital, Philadelphia, USA testified to The Committee as follows:

... obesity is in very large part a result of the way we live, of our lifestyles, and the most effective means for controlling obesity may lie in alterations of our lifestyles. (Source: Diet Related to Killer Diseases, II, Part 2. Obesity, February 1 & 2, 1977, p. 77.)

Dr. George A. Bray, Harbor General Hospital, Torrance, California, USA, on the same day testified:

I think a diet in and of itself is insufficient, that it needs to be coupled with some changes in lifestyle, which led to the obesity problem, of which nutrition is just one part. (Source: Diet Related to Killer Diseases, II, Part 2. Obesity, February 1 & 2, 1977, p. 209.)

Cardiovascular disease

Although 'The Report' (p. 45) exonerates sucrose from being a factor in heart disease, in its keynote statements, page 9, third paragraph, it relates sucrose to six of the ten leading causes of death including heart diseases.

The view of the scientific community is illustrated by Dr. Francisco Grande, School of Public Health, University of Minnesota, USA, as recorded in The Committee Hearings:

It has been claimed that sugar (sucrose) is an important factor in the development of CHD in man. . . . Two thorough reviews of this problem have appeared in 1971. One of the reviewers [Professor A. R. P. Walker] concluded that "although evidence is incomplete, such evidence as is available does not significantly incriminate sugar." The other [Professor Ancel Keys] concludes that "the theory is not supported by acceptable clinical, epidemiological, theoretical or experimental evidence." (Source: 6A. Appendix to Nutrition and Health, June 21, 1974, p. 3060 & 3061.)

General

The Foundation, in addition to its research program, has every year organized symposia-type conferences grouping panels of highly reputed scientists to discuss specific aspects of sucrose consumption and public health. In March of 1976 the Foundation invited six outstanding world scientists—each recognized authorities in their field of activity—to present to its membership current concepts about the relationship of dietary sugar (sucrose) to medical problems. Following individual presentations, they met among themselves and recorded their ideas and conclusions in a formal statement, see Appendix B. It is significant that these learned gentlemen are concerned with the large gap between the emotionally charged views of the antisucrose crusaders and the available scientific facts. In sharp contrast with 'The Report's' writers, they recommend much further research before dietary advice be given to the public. Their view is shared by Dr. Carolyn Berdanier, University of Nebraska, who testified:

. . . it is pretty early in the game to start making dietary recommendations with respect to sugar. We don't have all the facts in. . . .

"Until we are able to sort people out as to whether they are carbohydrate sensitive or insensitive, we should not attempt to set intake levels except in the case of the young. It is my personal opinion that broad recommendations for adults are, at this point, not warranted. (Source: Part 2. Sugar in Diet, Diabetes, and Heart Diseases, April 30, and May 1, 2, 1973, p. 157.)

'The Report' is at variance with two very considerable recent studies. First, a Report on Preventive Medicine issued in Britain by the Social Services and Employment Sub-Committee of the Expenditure Committee of the House of Commons. Issued on February 17, 1977, and based on hearings during the period from a wider range of witnesses and written evidence than was covered by the Staff of your Committee, we would make particular reference to the summary in Paragraphs 239 to 260 on pages lxxix to lxxiii which state inter alia:—

The 1976 Report of a Working Party of the Royal College of Surgeons and the British Cardiac Society on Prevention of Coronary Heart Disease supported the fat theory [rather than Dr. Yudkin's sugar theory] * as did the British Dietetic Association; the British Medical Association told the Sub-Committee that on balance they believed it [the fat theory] * to be winning. (* Bracketed words taken from preceding paragraph.)

They make *no* recommendations about sugar in this connection.

Second, there is the Report, "Evaluation of the Health Aspects of Sucrose as a Food Ingredient", prepared for the Bureau of Foods, Food & Drug Administration, Department of Health, Education and Welfare, Washington, D.C. by the Life Sciences Research Office, Fed-

eration of American Societies for Experimental Biology, (1976) In the opinion of this eminent body:

Broad generalizations based upon the inconclusive evidence now available must be made and viewed with caution. (p. 13.)

After surveying the whole range of possible connections between sucrose and disease, this Report concludes:

Other than the contribution made to dental caries, there is no clear evidence in the available information on sucrose that demonstrates a hazard to the public when used at the levels that are now current and in the manner now practiced. However, it is not possible to determine without additional data, whether an increase in sugar consumption—that would result if there were a significant increase in the total of sucrose, corn sugar, corn syrup, and invert sugar, added to foods—would constitute a dietary hazard. (p. 14 & 15.)

Conclusion

As an official document from such a prestigious body as the United States Senate, and although intended for the U.S. public, 'The Reports' impact will be worldwide. As it will be quoted by the media, politicians and health educators, its influence will be enormous and its recommendations, therefore, must be unassailable.

We very respectfully submit that 'The Report' is unfortunate and ill-advised. It does not reflect the testimonies of the experts given at The Committee Hearings and is in disagreement with the consensus of scientific thinking. It will confuse and mislead the public and bring discredit to The Committee members in the scientific community.

For these reasons, we respectfully suggest that The Committee should seek a wider and more judicious examination of the whole evidence available by scientists from the many reputed national health institutes. In this regard we join Dr. Johanna Dwyer who stated at The Committee Hearings:

I trust that before settling on dietary goals for the United States that the considerable expertise of the National Institutes of Health, The National Academy of Sciences and other government agencies will be harnessed to make sure that the suggested goals are firmly based in scientific evidence, realistic in terms of predicting possible benefits of such regimes. (Source: Part 2. Obesity, February 1 and 2, 1977, p. 71.)

THE INTERNATIONAL SUGAR RESEARCH
FOUNDATION, INC.

K. C. SINCLAIR, Chairman.
G. SARAULT, President.

APPENDIX A

The International Sugar Research Foundation, incorporated in 1968, succeeded the Sugar Research Foundation, founded in 1943. Its membership is composed of sugar industries in the U.S.A., the United Kingdom, Ireland, Belgium, Canada, the Dominican Republic, Rhodesia, South Africa and Venezuela. It is directly concerned with the role of sucrose in nutrition and the relation between its consumption and public health. It devotes some \$100,000 per year in support of related research projects carried out by scientists, recognized as experts in their field, and working in reputed institutions in many parts of the world. Additionally, it organizes symposium-type conferences at which internationally known researchers present their latest findings and express their views on the same subject.

ISRF

APPENDIX

SPECIAL EDITION NO. 1.

May 1977

SUCROSE AND HEALTH

SCIENTISTS' STATEMENT

March, 1976

Palm Beach, Florida

In March, 1976, Professor M. Apfelbaum, Hopital Bichat, France; Professor W. J. H. Butterfield, Regius Professor of Physic, Cambridge University, England; Professor Ian Macdonald, Guy's Hospital Medical School, England; Dr. P.J. Nestel, Head, Dept. of Cardiovascular Metabolism and Nutrition, Baker Medical Research Institute, Australia; Professor E. Pfeiffer, Universitat Ulm, Germany; and Professor T. B. Van Itallie, Department of Medicine St. Luke's Hospital Center, U.S.A., were invited by the International Sugar Research Foundation (ISRF) to present to its membership current concepts about the relationship of dietary sugar (sucrose) to medical problems.

Because the scientists were encouraged by assurances from the Foundation that its membership wanted a completely objective discussion of current information about the health implications of sugar with no attempt to minimize scientific reports unfavourable to this foodstuff, and because they work in widely separated areas of the globe, they welcomed the opportunity to meet with their colleagues to review this rapidly evolving and controversial subject.

At a meeting with the ISRF in open session, the scientists, each contributing information in which he is particularly knowledgeable, considered sugar generally in relation to three major health problems: obesity, diabetes and coronary heart disease. The scientists then met among themselves and decided that it would be useful to record their ideas and conclusions; hence the following statement.

"Before discussing current views about the role of sucrose in the etiology of obesity, diabetes mellitus and coronary heart disease, we should like to emphasize that we are not persuaded by certain pronouncements that attribute these conditions to a single cause. We consider these disorders to be multifactorial, the result

*** THE BULLETIN ***

A SUMMARY OF ISRF ACTIVITIES
AND DEVELOPMENTS OF INTEREST TO THE SUGAR WORLD

Published by The International Sugar Research Foundation, Inc.

of complex interactions of factors and events in any individual's life.

"It also seems important to point out that in affluent societies, where food is now readily available and over-consumed, there is competition between the various food industries for the market, intensified by the widespread current advice to individuals generally to reduce energy consumption. On the other hand, it must not be forgotten that sugar is an important, even vital, element in the diets and economies of developing tropical countries. The following remarks about obesity, diabetes and heart disease should, therefore, be taken in particular relation to affluent Western societies.

"Sugar is conventionally thought to play a significant role in the development of obesity on the grounds that its palatable taste may impel individuals to consume calorie-rich sugar-containing foodstuff in the absence of physiological hunger. It is well recognized that many persons routinely consume substantial quantities of sweetened foods after the completion of an adequate meal. The extent to which such practices contribute to obesity as a public health problem is poorly understood. In affluent societies, in which the calorie supply is unlimited and physical activity at an undesirably low level, sugar is undoubtedly one of a number of dietary factors that can contribute to obesity. However, there is no sound scientific evidence to indicate that, on the average, adults who overeat and gain excess weight obtain a disproportionate share of the extra calories from sugar.

"Some children, adolescents and adults undoubtedly find sweet-tasting foods of various kinds so irresistible as to make control of energy intake very difficult. Thus, it may prove helpful to develop a technique for identifying at an early age those individuals who are most likely to abuse sucrose. The best way to help obese or potentially obese persons cope with the problem of calorie control is to identify those foods (including sucrose-sweetened foods) that provide the greatest incentive to overeat. Once such target foods are known, the subject at risk can be retrained in their use.

"In many societies, recent urbanization and modernization have been accompanied by sharp increases in both sugar consumption and diabetes. In several genetically-susceptible animal strains obesity and diabetes have been produced by overfeeding of simple carbohy-

drates. But diabetes has also been produced in certain susceptible animals with diets high in fat or protein. In genetically-selected caged rats diabetes has been produced with diets containing 40-70% of calories as sucrose or other sugars. Weights of these animals were not increased at the onset of diabetes. These observations have led some physicians and nutritionists to conclude that sugar consumption may be one of the significant causes of diabetes. However, other contrary evidence has been presented in man and animals. For example, in some animals diabetes has been produced by diets high in fat and low in carbohydrate. Some human societies have high rates of diabetes despite low levels of sugar consumption, and diabetes is uncommon in some communities despite high levels of sugar intake.

"Therefore, a substantial majority of informed scientists in the field regard this an open question. Present evidence does not conclusively incriminate or entirely exonerate sugar in this respect. The degree of fatness appears to be the most important nutritional factor in determining the risk of diabetes, irrespective of the source of the calories.

"A common view among informed scientists is that consumption of sucrose and other sugars might, under certain special circumstances, enhance susceptibility to diabetes, while being innocuous under other conditions. The scientific community deems this an important issue. Further studies in animal and man would be useful. These investigations should include studies of the interrelationships between genetic factors and the responses to generous levels of dietary sugars in animals and man.

"Claims that sucrose is a direct and specific cause of coronary heart disease cannot be scientifically substantiated. Many factors contribute to the development of coronary heart disease including heredity, high blood pressure, high serum lipids, smoking, lack of exercise, obesity and diminished glucose tolerance. Since the consumption of excessive calories may lead to the development of some of these risk factors, it may also contribute to coronary heart disease. Therefore, it seems at this time that a possible role for dietary sucrose is as one of the sources of excess calories.

"There is no consistent evidence that persons with coronary heart disease eat more sucrose than those apparently free of disease, nor that excessive coronary

heart disease is found in all populations having a high intake of sugar.

"To conclude, we deplore the over-simplified and often misleading statements about sucrose that are so prevalent in the lay press today. We believe that the public is entitled to receive information about sucrose which is, as far as possible, impartial, accurate and in proper perspective; and we have striven to achieve such balance in the foregoing brief summary of our views. Individual members of society should be protected from the attractive notion that if they simply avoid a single dietary item, such as sugar, or eat some other dietary foodstuff, they will automatically be protected from obesity, diabetes or coronary heart disease. Much further research is needed in this broad field so that dietary advice to individual patients and to the public can be firmly grounded in scientifically verifiable facts.

As an addendum to their statement, the scientists pointed out:

"It is not our intention to make value judgments about sugar or the role it should play in the diet. Judgments about how much or how little sugar people should consume (as in the case of any important nutrient) are necessarily based on a complex array of considerations which cannot be taken up in such a brief communication. What particularly concerns us here is the large gap that exists between certain emotionally charged views which have been expressed about the putative role of sugar as a disease-promoting foodstuff and the available scientific facts."

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NATIONAL CANNERS ASSOCIATION,
Washington, D.C., July 8, 1977.

Senator GEORGE MCGOVERN,
Chairman, Select Committee on Nutrition and Human Needs,
U.S. Senate, Washington, D.C.

DEAR SENATOR MCGOVERN: On behalf of its members who account for more than 90 percent of U.S. canned food production, the National Canners Association wishes to take issue with some of the conclusions reached in your staff report "Dietary Goals for the United States."

First, we wish to point out the importance of canned foods in the American diet. The following figures show per capita consumption in pounds of fruits and vegetables by product form in farm weight equivalent for 1975, the latest year for which data is available.

	Fresh	Canned	Frozen	Dried
Fruits.....	95.1	47.2	¹ 60.4	10.6
Vegetables.....	100.8	102.5	19.9	14.5

¹ 93.5 percent is frozen concentrated citrus juices (56.5 lb).

Please note that canned fruit consumption represents nearly one-fourth of total United States dietary intake of fruits. Canned vegetables account for 45 percent of per capita vegetable consumption and are virtually equal to fresh vegetable consumption.

In addition, Americans consume great quantities of canned dairy products, meat, poultry, sea foods, soups, and infant foods, as well as a variety of specialty foods and combinations.

The annual per capita consumption of canned foods is approximately 150 pounds—slightly over 10 percent of total per capita food consumption.

Clearly, canned foods represent a significant portion of the U.S. food supply and are relied upon by consumers as valuable for dietary and nutritional requirements.

Without canning, much of the nation's raw agricultural production would be lost. This method of food preservation makes available year-round a wide variety of food products when the fresh equivalent is not available.

With these facts in mind, we wish to point out several statements in "Dietary Goals for the United States" that we consider erroneous or misleading:

Page 21.—"* * * fresh fruits and vegetables in the supermarket may have undergone nutrient-depletion in shipping and storage, and consequently frozen varieties may provide equivalent or better nutritional values."

Comment.—Canned fruits and vegetables are processed within hours of harvesting, thus important nutrient levels remain high when the canning process is completed. These nutrients, for the most part, remain an integral part of each canned food item. The report should recognize the nutritional values of canned foods, as well as those of frozen products.

Pages 21 and 22.—"Consequently, it would seem advisable to create at least an even balance in the diet between the fresh and frozen produce (Canned produce has significant nutritional value but is generally thought to have retained less nutrients than frozen or fresh.) In addition, it would appear to be prudent to increase consumption of potatoes and dark green leafy vegetables because of nutrient content and the varieties of fiber they may offer."

Comment.—Again, the report should recognize the advisability of an even balance in the diet among fresh, frozen and canned foods. It must be remembered that canned foods have been fully processed and are ready to eat; fresh and frozen foods need to be cooked. Therefore, nutrient losses that occur during preparation for the table must be considered when making comparisons with canned foods. A recent IFT technical article stated "Because of the large losses that occur in the home, the actual vitamin content of table-ready foods is frequently about the same regardless of the type of processing or lack of processing the food has undergone."

Page 22.—"Highly-refined fruits and vegetables generally should not be viewed as nutritional equivalents or substitutes for the same food in its fresh form. For example, Table 2 shows that potato chips and dehydrated potatoes should not be thought of as the nutritional equivalent of fresh, baked potatoes. In addition, it is apparent that potato chips carry significantly more fat than the baked or mashed form: potato chips are 40 percent fat compared to .1 percent fat in baked potatoes."

Comment.—Canned foods should certainly not be confused with such products as potato chips. Canned fruits and vegetables are not "highly refined," as the report suggests, but receive only the application of heat necessary for safe, proper preservation. A minimum of additives are employed in processing fruits and vegetables by the canning industry. Canning products are basic foods, naturally preserved.

Page 22.—"Finally, the use of fresh produce also removes food from the processing system in which a sizeable portion of food prices may result from non-food costs such as packaging, advertising and any added costs that may accrue to imperfect competition in food manufacturing * * *"

Comment.—The report suggests time and time again that fresh foods are preferable, not only for their nutritional value, but also because processed foods are higher in cost. In fact, canned foods are often the lowest cost choice for consumers. For example, the July 1977 issue of Consumer Report compared fresh, frozen and canned green beans and concluded that the canned beans were the cheapest of all, averaging 3.1 cents per ounce. Fresh beans were next in price, averaging 3.8 cents an edible ounce. Plain frozen beans cost an average of 4.2 cents an edible ounce. Consumer Report noted that the fresh beans were bought in the peak season, adding that their "price may go quite a bit higher out of season."

Consumer Report said its cost finding should provide a rule of thumb for judging prices of other vegetables. "Canned will almost always be cheapest," the magazine said.

Consumer Report added: "Canned vegetables are not only the cheapest. They're the most convenient. They store easily. They keep

longer than frozen vegetables (three years as opposed to one, under optimum conditions). And all you have to do is heat them in the brine they come in."

Surely, a report by your committee should recognize the economy of canned products, particularly for low-income families, which may not be able to afford more expensive forms of food.

Page 24.—" * * * Given the need to maximize micro-nutrient availability for those on reduced diets; the need to ensure adequate nutrient availability to those who do not widely vary their diets; and the need to maximize the nutritional power of the food supply; it would seem prudent not only to increase use of fresh foods but also those undergoing the least processing."

Comment.—Once again, the committee staff should understand that canned foods received only the amount of processing necessary to render them bacteriologically sterile and, therefore, shelfstable for an indefinite period of time.

We also wish to take issue with comments in the section of the report dealing with reduction of salt consumption. Basically, we rely upon comments already submitted by the American Medical Association and by the Salt Institute. In effect these comments suggest that the role of salt in hypertension is very controversial and that most people need not be concerned about dietary salt intake.

Consumers prefer canned vegetables that are lightly salted and no doubt add as much or more salt to fresh and frozen vegetables in preparation or at the table.

For those who need to restrict sodium intake, the canning industry provides a wide variety of low-sodium products.

We are providing to your committee staff complete studies and reports supporting each of the points that we have made here. A bibliography of these materials is attached.

I sincerely hope that these comments will be carefully weighed in any revision of "Dietary Goals of the United States," or in any similar studies that your committee might undertake.

Sincerely,

IRA I. SOMERS, Ph. D.,
Executive Vice President.

Enclosure.

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STATEMENT ON DIETARY GOALS FOR THE UNITED STATES
BY THE NATIONAL DAIRY COUNCIL, ROSEMONT, ILL.

National Dairy Council (NDC) welcomes the opportunity to comment on the document "Dietary Goals for the United States," published in February 1977. NDC is a nonprofit educational-scientific organization, supported by producers, processors and handlers, and equipment manufacturers and jobbers in the dairy industry. NDC

conducts a nutrition research program which serves as a scientific base for its nutrition education and nutrition communications programs. Dairy Council is both a national and a community effort, with NDC directing the national programs, and approximately 275 regional, State and community Dairy Council professional staff bringing these programs and services to their respective areas.

NUTRITION AS A NATIONAL ISSUE

During the last few years, nutrition has received increasing attention from all sectors of society. More and more, there is a growing recognition of the need to develop basic policy decisions which would address a wide range of nutrition concerns. In 1974 the National Nutrition Consortium prepared a working paper, published by the U.S. Senate Select Committee on Nutrition and Human Needs, which broadly defined the essential components of a national nutrition policy [1]. In 1976 the Office of Technology Assessment (OTA), U.S. Congress, laid groundwork for defining current as well as emerging issues for use in formulating basic policies affecting the food system of the Nation. National Dairy Council was one of the organizations requested by OTA to submit specific recommendations for a national policy on food, nutrition and health.

The publication in early 1977 of the report "Dietary Goals for the United States" is an effort by the staff of the Select Committee on Nutrition and Human Needs to work toward providing practical dietary guides to the individual consumer and setting national dietary goals for the country. However, the Society for Nutrition Education [2] noted that the evidence on which the proposed goals are based is "limited to epidemiological data and food disappearance studies which result in population needs rather than individual goals."

We believe it is highly questionable that adherence to the changes in dietary composition recommended in the report would indeed result in a reduction in the incidence of heart disease, cancer, cerebrovascular disease, diabetes, arteriosclerosis and cirrhosis of the liver. We agree with the American Medical Association [3] that " * * * it would be inappropriate at this time to adopt the proposed national dietary goals as set forth in the Report on Dietary Goals for the United States. The evidence for assuming that benefits to be derived from the adoption of such universal dietary goals as set forth in the Report is not conclusive and there is a potential for harmful effects from a radical long term dietary change as would occur through adoption of the proposed national goals".

The inconclusiveness of the evidence may be illustrated by the current state of knowledge of coronary heart disease. The lack of agreement on a common course of action to take in the prevention of coronary heart disease is due to the fact that it is a complex multifaceted disease process. Strasser [4] has listed 37 different variables which may be correlated with atherosclerosis. Kritchevsky [5] uses the "pie chart" concept, with the relative size of the different "wedges" or factors being different for each individual. Each individual reacts to different factors in different ways. Moreover, factors which are of a high-risk type on a population basis may not be so on an individual

basis, and vice versa [6]. Thus, recommendations for coronary heart disease prevention should be considered only in the context of all possible causes, and on an individualized basis.

NHLBI CLINICAL TRIALS

Data concerning the possible benefit of fat-modified diets in lowering the incidence of CHD in the population at large are largely equivocal or even conflicting. The National Heart, Lung and Blood Institute is currently supporting large scale clinical trials such as the Multiple Risk Factor Intervention Trial (MRFIT) and the Lipid Research Clinics Coronary Primary Prevention Trial (LRC-CPPT) to investigate questions that have remained unanswered. The goal of the MRFIT program is to determine whether the combined reduction of three major risk factors for CHD (high blood cholesterol levels, high blood pressure and smoking) in persons in a higher risk segment of the U.S. population but without evidence of prior or present cardiovascular disease, would prevent or reduce the incidence of first heart attacks and premature death. The LRC-CPPT on their other hand, is testing whether lowering cholesterol in hypercholesterolemic but otherwise healthy subjects will reduce or slow the development of premature coronary heart disease. This trial is actually testing the lipid hypothesis. The mere fact that these trials are being conducted is evidence of insufficient knowledge as to the best course of action to prevent coronary heart disease in the general population.

TECUMSEH STUDY

The Tecumseh study has revealed that serum cholesterol and triglyceride levels are unrelated to quality, quantity, or proportions of fat, carbohydrate or protein consumed [7]. Instead, the findings reveal that serum cholesterol and triglyceride levels among Americans are more dependent on degree of adiposity than on frequency of consumption of fat, sugar, starch or alcohol [8].

OBESITY

Rather than focusing on individual components of the diet, present knowledge indicates that a more productive approach in improving the health of the American population is to deal with the problem of obesity. In the United States today the general tendency to overconsumption of calories, coupled with minimal physical activity, has predisposed many to overweight and its complications. Obesity is a common denominator of many nutrition-related public health problems. It is a risk factor in cardiovascular disease, hypertension, atherosclerosis, hernia, gallbladder disease, diabetes mellitus and liver diseases [9] and aggravates osteoarthritis [10]. Obesity also may be a risk factor in carcinogenesis. In humans, epidemiological studies have shown that obesity is correlated with cancers of the intestinal tract, liver, genitourinary tract, uterus, gallbladder and breast [11]. Studies with animals show that within each group of animals receiving identical diets, the incidence of every tumor type was consistently greater in heavy rats than in lean rats [11]. Of all the dietary alterations

studied in experimental animals, caloric restriction either through underfeeding or through restriction of dietary carbohydrate, has had the most regular influence on the genesis of tumors. Chronic caloric restriction inhibits the formation of many types of tumors, decreasing their incidence and delaying the time at which they appear [11].

There appears to be a general consensus in the medical and scientific community that the greatest impact of nutrition-related measures on the health of the general population is through prevention or treatment of obesity, as evidenced by the following statements:

(a) Society for Nutrition Education, Board of Directors [2]

"* * * obesity is a major health problem, one related to increased risk from several other diseases, e.g., hypertension. Obesity is directly related to food intake in excess of energy output needs. For this reason, we feel that general goals for calorie consumption are important."

(b) George Cahill, M.D., Joslin Institute, Boston, Mass. [12]

"* * * we know that 90 percent of middle-age people who have diabetes could have their glucose tolerance reduced, or many even corrected back to normal, by simply weight reduction alone..."

(c) Jeremiah Stamler, M.D., Northwestern University Medical School, Chicago, Ill. [13]

"* * * our nation is second to none among the industrialized countries of the world in regard to calorie excess (i.e., overage of calorie intake in terms of energy expenditure), so that gross obesity is a very common phenomenon in our population, not only among the middle-aged and elderly, but even among our children, teen-agers and young adults * * *. The importance of this fact is underscored by the related finding that obesity is associated with significant increase in probability of developing two of the major risk factors, i.e., hypercholesterolemia and hypertension, especially when obesity is already manifest in the teens or young adulthood."

(d) Fredrick J. Stare, M.D., Ph.D., Harvard University, Boston, Mass. [14]

"* * * the most important nutritional problem in our country [is] eating and drinking (alcoholic beverages) too much, and not using enough of these extra calories in muscular activity. Result—obesity."

(e) Philip L. White, Sc.D., American Medical Association, Chicago, Ill. [15]

"Would it not be better to concentrate our resources on the control of obesity and the promotion of fitness?"

The main dietary determinant of obesity is total amount of calories (energy) and not their source (i.e., whether or not the calories are provided by carbohydrate, fat or protein) [3].

National Dairy Council agrees with the American Medical Association [3] that:

"* * * individual programs to prevent or to treat obesity through decreased calorie intake along with programs aimed at improving physical fitness would be the most effective means of improving the health of our American citizens."

INPUT FROM PROFESSIONAL COMMUNITY AND THE FOOD INDUSTRY

Any set of national dietary goals will have far-reaching effects on all segments of society. It is, therefore, essential that the professional community and the food industry at the highest levels be involved in the formulation of these goals in order to assure that the goals are firmly based on scientific evidence, represent an objective assessment

of the current state of knowledge, and can be implemented from a practical standpoint. Representation from the food industry and from the following groups must be sought in such an endeavor :

- American Academy of Pediatrics.
- American Dietetic Association.
- American Heart Association.
- American Institute of Nutrition.
- American Medical Association.
- American Society for Clinical Nutrition.
- American Public Health Association.
- Food and Drug Administration.
- Food and Nutrition Board, National Academy of Sciences/National Research Council.
- Institute of Food Technologists.
- National Institutes of Health.
- Society for Nutrition Education.
- U.S. Department of Agriculture.

With the endorsement of the dietary goals by these groups, the goals will have a broad base of support, which will pave the way for nationwide adoption. The dietary goals as formulated by the staff of the Select Committee on Nutrition and Human Needs do not now have such a support. We, therefore, urge that they be withdrawn.

SUMMARY

1. It is highly questionable that adherence to the changes in dietary composition recommended in the report on Dietary Goals for the United States would indeed result in a reduction in the incidence of heart disease, cancer, cerebrovascular disease, diabetes, arteriosclerosis and cirrhosis of the liver.

2. Obesity is the major nutritional problem in the United States today, being the common thread that runs through many public health problems.

3. The main dietary determinant of obesity is total amount of calories rather than dietary composition.

4. Individual programs to prevent or to treat obesity through decreased caloric intake along with programs aimed at improving physical fitness are the most effective means today of improving the health of the population.

5. We endorse the statement of the American Medical Association that:

(a) " * * * it would be inappropriate at this time to adopt the proposed national dietary goals as set forth in the Report on Dietary Goals for the United States. The evidence for assuming that benefits to be derived from the adoption of such universal dietary goals as set forth in the Report is not conclusive and there is a potential for harmful effects from a radical long term dietary change as would occur through adoption of the proposed national goals."

(b) [it is not] appropriate for the government to adopt national goals that specify such matters as the amount and proportions of total fat, type of fat, sugar, cholesterol, or salt content in the diets of the general public as these national goals advocate."

6. We recommend that the dietary goals as formulated by the staff of the Select Committee on Nutrition and Human Needs be withdrawn.

7. Formulation of national dietary goals should have the involvement and endorsement by the professional community and the food industry.

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CHAPTER IV

MAJOR REPORTS AND SURVEYS

A. UNIVERSITY OF OSLO SURVEY

1. STATEMENT OF SENATOR EDWARD M. KENNEDY RELEASING AN INTERNATIONAL SURVEY ON THE RELATIONSHIP OF DIET TO HEART DISEASE

Senator Edward M. Kennedy today released a world-wide survey of scientists that shows 99 percent are convinced that fatty diets contribute to heart disease.

He did so in advance of hearings Thursday by the Senate Select Committee on Nutrition, of which he is a member. Additionally, he is chairperson of the Subcommittee on Health and Scientific Research.

In releasing the report, Kennedy said :

The survey conducted by Dr. Karre R. Norum, Chairman of the Institute of Nutrition Research at the University of Oslo, involved 214 scientists from 23 countries. Preliminary findings were reported last month in the Journal of the Norwegian Medical Association but have not been published in the United States.

The survey is believed to be the first large scale measurement of scientific consensus on the relationship of diet to heart disease.

The scientists polled, Dr. Norum said in the report, include "the world's foremost clinicians, surgeons, pathologists, clinical geneticists and epidemiologists working in coronary research."

The survey finds that 99.4 percent of those responding believe there is a connection between diet and heart disease and that 91.9 percent believe that "knowledge about diet and coronary disease is sufficient to recommend a moderate change in the diet for the population in an affluent society."

The respondents gave the following priority to diet steps to reduce risk of heart disease:

1. Fewer calories;
2. Less fat;
3. Less saturated fat;
4. Less cholesterol;
5. More poly-unsaturated fat;
6. Less sugar;
7. Less salt;
8. More fiber; and
9. More starchy foods.

These priorities correspond with recommendations made in the Nutrition Committee's report published in January, 1977.

Discussing the priorities, Dr. Norum wrote:

Fewer calories, less fat and cholesterol in the diet were clearly given high priority by most. There was a certain disagreement on the importance of recommending a higher intake of polyunsaturated fat to prevent heart diseases.

And, he reports:

To the question whether the experts' personal knowledge had an effect on their personal diet over 90 percent answered "Yes."

Dr. Norum said in a telephone interview with the Nutrition Committee staff that the survey was conducted in response to meat industry arguments that there is considerable disagreement on the relationship of diet to heart disease.

In November, 1975, the Norwegian Ministry of Agriculture issues a report to that nation's parliament outlining nutritional guidelines for food policy and recommending among other things, limiting meat consumption as part of an effort to limit total fat and saturated fat intake.

The report said:

Meat production is a necessary link in the utilization of our resources. The present development tendencies imply that consumption will increase considerably in the next 10 to 15 years. Even if meat does not contribute as largely to fat consumption as, for example, margarine and whole milk, a continued increase in meat consumption will hardly be expedient, considering the desire to reduce the intake of fats. On the basis of a total assessment, an objective should therefore be to hold the consumption of meat per person at about the present level. A reduction in the fat content in meat should be aimed at.

The report also noted that a 1971 survey had found:

Our (Norway's) meat consumption was somewhat lower than in the other Nordic countries and much lower than in Great Britain, the USA and the Netherlands.

Dr. Norum concluded his report in the Norwegian Medical Journal saying:

Most experts are of the opinion that our knowledge affords the basis for a nutritional policy initiative. . . . Our politicians and authorities should see to it that the population makes use of this knowledge.

The survey was sent to scientists in the following countries:

Australia	Italy
Austria	New Zealand
Belgium	Norway
Canada	Poland
Denmark	Scotland
England	Spain
Finland	Sweden
France	Switzerland
Germany	United States of America
Iceland	U.S.S.R.
Israel	Venezuela

Dr. Norman's article from The Journal of Norwegian Medical Association is attached.

2. WHAT IS THE EXPERTS' OPINION ON DIET AND CORONARY HEART DISEASES?

(By Kaare R. Norum, Journal of the Norwegian Medical Association)

When the connection between disease and environmental factors is discussed among laymen, one of the usual arguments is that the experts are in disagreement so that sure conclusions are difficult to arrive at. There may be many reasons for this type of argumentation. It is not unusual that people without any real competence express themselves as if they had it. This applies especially to the nutrition sector where the level of knowledge, both in the population and among health staffers, is unfortunately low. Another reason may be that the experts are actually in disagreement. In both instances, dissimilar points of view and disagreement is interesting news and is often given great publicity in the mass media, whereby the people's impression of disagreement is enhanced.

Last fall, the connection between diet, cholesterol, and heart disease was again called into question. Articles in the technical press were much talked about and sometimes used as an argument against the professional basis for our official nutrition policy. To give an impression of what the experts' opinion is of diet and prevention of coronary heart disease, I sent a questionnaire to 214 outstanding women and men of science from 22 countries. The list of addressees consisted of leading researchers in lipid, lipoprotein, atherosclerosis and nutrition research. The selection was done by me and therefore of course was not done at random, but I sent the questionnaire to persons having been actively engaged in atherosclerosis problems in recent years. The questionnaire was sent out around December 15, 1976, and by February 15, 1977, 85 percent had answered without being reminded. The main questions and answers appear in the Table.

There is nearly unanimity on there being a connection between diet and development of coronary heart disease, between diet and plasma lipoprotein concentration and between plasma cholesterol and development of coronary heart disease. There is a certain disagreement on the role triglycerides play (Question 4). Thirteen percent of the researchers failed to answer this question, and many of them who answered "Yes" guarded against the connection being of a causal character. The same reservation may of course be made in regard to the connection in Questions 1, 2, and 3. That is why the answer to Question 5 is so important: 92 percent of the persons questioned are of the opinion that our knowledge about diet and coronary heart disease is sufficient for recommending, a moderate change in the diet of the population in a welfare society. Accordingly, it is the experts' opinion that the connection is of a causal nature. Those who answered "Yes" to Question 5 were asked what one should recommend to the population. Nine choices were set up for advice on diet, and the researchers were asked for priorities. The list of priorities was as follows: (1) Fewer calories; (2) less fat; (3) less saturated fat; (4) less cholesterol; (5) more polyunsaturated fat; (6) less sugar; (7) less salt; (8) more fiber, and the lowest priority was more starchy

foods. One priority did not exclude another, less fat might lead to more starchy foods, etc. The list shows only what the experts believe is most important to recommend to the population. Fewer calories, less fat than cholesterol in the diet were clearly given high priority by most. There was a certain disagreement on the importance of recommending a higher intake of polyunsaturated fat to prevent coronary heart diseases. To the question whether the experts' personal knowledge had an effect on their personal diet (Question 6), over 90 percent answered "Yes".

Over 80 percent believed that one or another form of "screening program" should be carried out to detect persons with a high risk of developing coronary diseases (Question 7). Those who answered "Yes", were asked to indicate what kind of standard examinations should be made. On this there were many different opinions, ranging from total screening of the whole population for lipids and blood pressure to merely examining those with a positive family medical history.

Nearly 90 percent knew their own serum lipid values (Question 8). As many as 85 percent did not smoke (Question 9), and over half of those who smoked did not use cigarettes.

This "poll" shows that there is strong agreement among the experts on some fundamental questions, and that there are dissimilar views in some areas. Most experts are of the opinion that our knowledge affords the basis for a nutrition policy initiative. They themselves have taken the consequences of their knowledge. Our politicians and authorities should see to it that the population makes use of this knowledge.

TABLE I

[In percent]

	Yes	No
1. Is there a connection between diet and development of coronary heart disease?.....	99.4	0.6
2. Is there a connection between diet and plasma lipoprotein concentration?.....	98.9	1.2
3. Is there a connection between plasma cholesterol concentration and development of coronary heart disease?.....	98.9	1.2
4. Is there a connection between plasma triglyceride concentration and development of coronary heart disease?.....	77.9	22.1
5. Is your knowledge of diet and coronary heart disease sufficient for recommending a moderate change in the diet of the population in our society?.....	91.9	8.1
6. Is your diet affected by your knowledge?.....	92.4	7.6
7. Should one or another form of mass examination be made to detect "high risk persons"?.....	82.6	17.2
8. Do you know your own serum lipid values?.....	87.6	12.4
9. Do you smoke?.....	14.8	85.4

[From JAMA, June 13, 1977—Vol. 237, No. 24]

3. EXPERTS LINK HEART DISEASE AND DIET

UNIVERSITY OF OSLO SURVEY

A sampling of medical scientists from 22 countries produced similar opinions about some aspects of dietary relationships with coronary heart disease.

Kaare Reidar Norum, M.D., chairman, Nutrition Research Institute, University of Oslo, Norway, sent a questionnaire last December

to 214 men and women around the world who are engaged in lipid, lipoprotein, atherosclerosis, and nutrition research.

Dr. Norum selected the recipients himself. He agrees that his was not a random sample, but notes (in the March 10 issue of *The Journal of the Norwegian Medical Association*) that these are "persons having been actively engaged in atherosclerosis problems in recent years." By mid-February, 85 percent of the addressees had responded. These are the results (translated by a staff member of the U.S. Library of Congress) :

Is there a connection between diet and development of coronary heart disease? Yes 99.4 percent. No 0.6 percent.

Is there a connection between diet and plasma lipoprotein concentration? Yes 98.9 percent. No 1.2 percent.

Is there a connection between plasma triglyceride concentration and development of coronary heart disease? Yes 77.9 percent. No 22.1 percent.

Is there a connection between plasma triglyceride concentration and development of coronary heart disease? Yes 77.9 percent. No 22.1 percent.

Is your knowledge of diet and coronary heart disease sufficient for recommending a moderate change in the diet of the population of our society? Yes 91.9 percent. No 8.1 percent.

Is your diet affected by your knowledge? Yes 92.4 percent. No 7.6 percent.

Should one or another form of mass examination be made to detect "high-risk persons"? Yes 82.6 percent. No 17.4 percent.

Do you know your own serum lipid values? Yes 87.6 percent. No 12.4 percent.

Do you smoke? Yes 14.8 percent. No 85.2 percent.

Dr. Norum told the U.S. Senate Select Committee on Nutrition that about half the respondents are from the United States.

Those researchers who considered their knowledge sufficient to recommend diet changes were given nine choices of dietary advice and asked to set priorities. Fewer calories, less fat, and less cholesterol in the diet got high priority from most. There was disagreement on the importance of recommending more polyunsaturated fat in the diet.

A statement from the office of Sen. Edward M. Kennedy (D-Mass), chairman of the Subcommittee on Health and Scientific Research, quoted Dr. Norum as saying in a telephone interview with the Nutrition Committee staff that "the survey was conducted in response to meat industry arguments that there is considerable disagreement on the relationship of diet to heart disease.

"In November 1975, the Norwegian Ministry of Agriculture issued a report to that Nation's parliament outlining nutritional guidelines for food policy and recommending, among other things, limiting meat consumption as part of an effort to limit total fat and saturated fat intake."

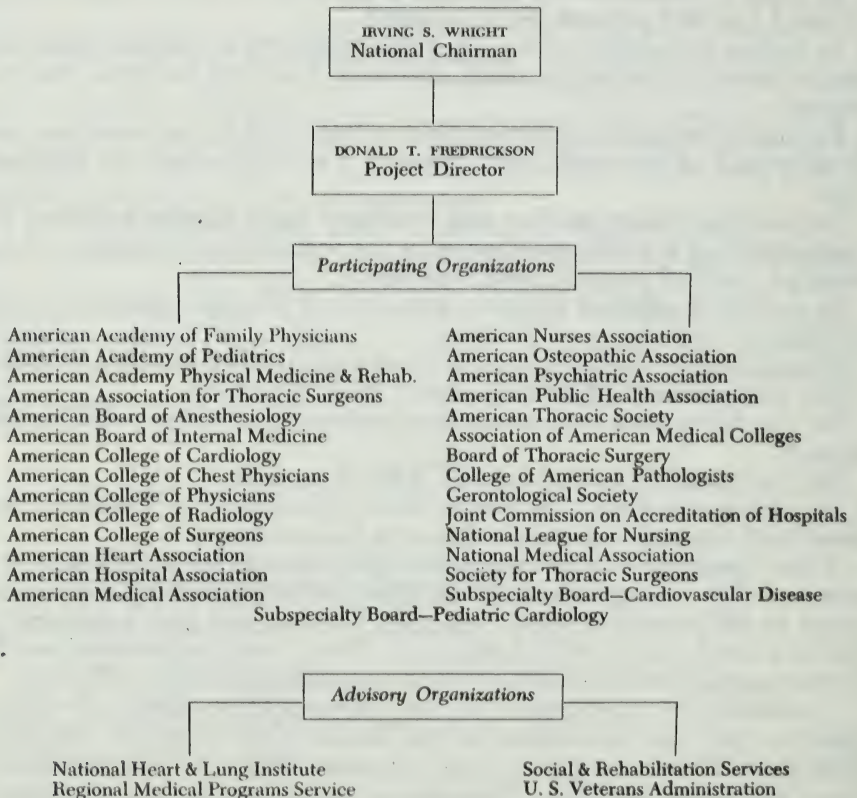
[From Circulation, Volume XLII, December 1970—Revised, April 1972]

B. REPORT OF INTER-SOCIETY COMMISSION FOR HEART DISEASE RESOURCES¹

PRIMARY PREVENTION OF THE ATHEROSCLEROTIC DISEASES

INTER-SOCIETY COMMISSION FOR HEART DISEASE RESOURCES

TABLE OF ORGANIZATION



IV. Recommendations for Primary Prevention

The Commission recommends the immediate and concurrent implementation of the following recommendations for the primary prevention of the atherosclerotic diseases:

¹ To obtain the complete report, address correspondence to Inter-Society Commission for Heart Disease Resources, 44 E. 23d Street, Suite 316, New York, N.Y. 10010.

National Policy Commitment to Strategy of Primary Prevention

A. The Commission recommends that a strategy of primary prevention of premature atherosclerotic diseases be adopted as long-term national policy for the United States and to implement this strategy that adequate resources of money and manpower be committed to accomplish:

Changes in diet to prevent or control hyperlipidemia, obesity, hypertension and diabetes

Elimination of cigarette smoking

Pharmacologic control of elevated blood pressure.

Definitive Field Trials of Primary Prevention

B. The Commission recommends that a Special Committee be established at a high level of the Federal Government to develop coordinated plans for large-scale, long-term trials to determine the effect of various interventions, particularly diet modification, on the rates of premature atherosclerotic diseases in the United States. The Commission recognizes that differences of opinion exist with regard to the likely beneficial effect of various types of change, particularly fat modification of the diet, on premature CHD in the United States. The public health importance of CHD makes it mandatory to conduct such trials.

The Commission further recognizes that even if planning were to start immediately, the American public would probably have to wait at least 10 years for results of these studies. At times urgent public health decisions must be made on the soundest evaluation and best judgment of available incomplete evidence. The formulation of such judgments was the charge to the Commission. Therefore, the Commission recommends that actions with regard to the reasonable and safe changes described below be promptly implemented at the same time that a trial is being planned and implemented.

TABLE 15.—ESTIMATION OF NUMBER OF EVENTS AND DEATHS THAT WOULD BE PREVENTED PER YEAR BASED ON EFFECTIVENESS OF THE PROCEDURE AND PERCENTAGE OF THE POPULATION INCLUDED: WHITE MALES AGE 35 TO 64 (92)

Percentage of population accepting modification	Potential effectiveness and number of events prevented							
	10-percent effective		20-percent effective		50-percent effective		100-percent effective	
	Cases prevented	Deaths prevented	Cases prevented	Deaths prevented	Cases prevented	Deaths prevented	Cases prevented	Deaths prevented
10 percent.....	3,000	600	6,000	1,200	15,000	3,000	30,000	6,000
20 percent.....	6,000	1,200	12,000	2,400	30,000	6,000	60,000	12,000
50 percent.....	15,000	3,000	30,000	6,000	75,000	15,000	150,000	30,000
100 percent.....	30,000	6,000	60,000	12,000	150,000	30,000	300,000	60,000

TABLE 16.—ESTIMATED RELATIVE REDUCTION IN CORONARY HEART DISEASE INCIDENCE (v) ASSOCIATED WITH RELATIVE REDUCTION IN SERUM CHOLESTEROL (uv) (76)

Relative decrease in serum cholesterol (u)	Relative disease in coronary heart disease incidence (v)	Relative decrease in serum cholesterol (u)	Relative decrease in coronary heart disease incidence (v)	Relative decrease in serum cholesterol (u)	Relative disease in coronary heart disease incidence (v)	Relative decrease in serum cholesterol (u)	Relative decrease in coronary heart disease incidence (v)
0.01	0.026	0.14	0.330	0.27	0.567	0.39	0.731
.02	.052	.15	.351	.28	.583	.40	.743
.03	.078	.16	.371	.29	.598	.41	.754
.04	.103	.17	.391	.30	.613	.42	.765
.05	.128	.18	.410	.31	.627	.43	.776
.06	.152	.19	.429	.32	.642	.44	.786
.07	.176	.20	.448	.33	.655	.45	.796
.08	.199	.21	.466	.34	.669	.46	.806
.09	.222	.22	.484	.35	.682	.47	.815
.10	.244	.23	.501	.36	.695	.48	.824
.11	.267	.24	.518	.37	.707	.49	.833
.12	.288	.25	.535	.38	.720	.50	.842
.13	.310	.26	.551				

Note: Values of v were obtained from the relationship, $v=1-(1-u)^{2.64}$ described in reference (93).

These data illustrate the potential for prevention, and the possibility of achieving declines in CHD morbidity and mortality as projected in the preceding table (table 15). For example, a 10-percent reduction in serum cholesterol level of the U.S. population ($u=0.10$) is estimated to yield a 24.4-percent decrease in CHD incidence ($v=0.244$).

*Diet and Food Modifications*¹

C. The Commission recommends the following modifications of diet for the general public, and particularly for individuals with marked increase in risk of premature atherosclerotic diseases.

(1) *Calorie Intake Be Adjusted to Achieve and Maintain Optimal Weight.*—Correction of obesity is known to be frequently associated with significant control of certain CHD risk factors, e.g., fall in blood pressure of some hypertensive patients, decrease in blood glucose levels in some patients with maturity-onset diabetes, decline in elevated serum triglyceride levels. It is generally agreed that this measure is a reasonable and safe aspect of any prophylactic regimen.

(2) *Reduction of Dietary Cholesterol to Less Than 300 mg Per Day.*—The average daily diet in the United States contains approximately 600 mg of cholesterol. Substantial reduction in amount of cholesterol in the diet has been found to lower concentration of cholesterol in the serum of most people. Since cholesterol is present in many protein sources of high biological quality, careful planning is necessary to lower intake of cholesterol without impairing intake of protein.

(3) *Substantial Reduction of Dietary Saturated Fats.*—This change will lower concentration of cholesterol in the serum of most people. The ideal quantity of fat needed in the diet is not known but moderation in intake is considered desirable, i.e., less than 35 percent of total calories from all fats. Intake of less than 10 percent of total calories from saturated fats is of critical importance for attainment of optimal serum cholesterol levels for most people. Unsaturated fats may be used in moderation to replace a portion of the saturated fats, i.e., 10 percent of calories from mono- and up to 10 percent for polyunsaturated fats. With proper control of saturated fat, cholesterol and calorie intake, as recommended above, ingestion of large amounts of polyunsaturated fats—i.e., 10 percent or more of total calories—is generally not necessary for control of serum lipid levels. International data indicate that populations with low serum lipid levels and low CHD mortality rates

¹ See Annex 1.

habitually consume diets low in saturated fat and cholesterol, and low or moderate in total fat and polyunsaturated fat—not high in the latter.

With these dietary principles, requirements for optimal nutrition can be met for all sectors of the population, including infants, children, adolescents, pregnant and lactating women, and older persons.

For individuals with severe hyperlipidemia—hyperlipoproteinemia of various types, their physicians will often deem it appropriate to prescribe more extensive and specific nutritional and drug therapy.

Changes in the environment to aid the American people to improve their diet should be a major aspect of this effort at prevention. Recent research has shown that it is entirely possible to prepare foods commercially in ways that will contribute substantially to the control of hyperlipidemia. In the National Diet-Heart Study, many foods were prepared with sizeable reductions in content of total fat, saturated fat, cholesterol and calories. This was done with dairy and meat products, baked goods, frozen desserts and other foodstuffs. It was demonstrated that modified foods can be made in forms that are highly acceptable to the consumer.

The Commission therefore recommends that the food industry be encouraged by the medical profession and the government and supported by the general public to make available leaner meats and processed meats, dairy products, frozen desserts and baked goods reduced in saturated fats, cholesterol and calories, and visible fats and oils (margarines, shortenings, mayonnaises, salad dressings, oils) of low saturated fat and cholesterol content.

For this purpose the Commission further recommends that comprehensive review and revision of policies and regulations be conducted to aid in accomplishing the following objectives:

Meats

a. The production of red meat low in saturated fats and meat products (e.g., sausages, hot dogs and cold cuts) low in saturated fats and cholesterol. In the United States it is widespread practice to keep beef cattle in stalls and feed them heavily to produce meat with a high fat content. To produce red meat low in saturated fats will require changes in cattle breeding and feeding practices. Processed meat products (sausages, hot dogs, cold cuts, etc.) low in saturated fats and cholesterol can be produced so that they are completely acceptable to the consumer. At present, processed meats cannot be made with vegetable oils because of U.S. Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), state and/or local regulations which define this as adulteration. It is necessary therefore to encourage:

Development of strains of animals that convert higher proportions of feed to protein rather than fat.

Shift to range feeding with earlier slaughter of cattle to yield leaner animals.

Modernization of laws and regulations relating to the definition of meat products.

Further development of high quality vegetable protein products.

Development of an intensive educational program concerning the cooking of lean meats to assure their optimal palatability and acceptability without the use of added saturated fats.

Dairy Products

b. Reduction in saturated fat and cholesterol content of dairy products.

Industry and government should review and establish policies (including pricing policies) that will encourage development of low-fat, low-cholesterol milk and milk products, and use of cows producing large amounts of high protein, low-fat milk. Wholesale pricing of dairy products is still based on butter fat content, a practice persisting from the days when measurement of butter fat was used to detect skimming or watering of milk.

The dairy industry should be helped and encouraged to develop techniques for reducing saturated fat and cholesterol in cheeses of all varieties. Total fluid milk consumption in the United States is decreasing while consumption of cheese is steadily increasing. At current levels of consumption significant control of hyperlipidemia seems unlikely unless composition of cheeses can be altered. The National Diet-Heart Study demonstrated that limited progress has been made in this area, and further progress certainly is possible.

Industry should be stimulated to develop creamers low in total fats, saturated fats and cholesterol. Changes in labeling and advertisting of cream substitutes are needed so that their actual fat composition is clear.

The so-called non-dairy-fat creamers currently on the market present a special problem. These products are characterized by a high content of coconut oil and/or hydrogenated vegetable oil and therefore of saturated fat. Coconut oil is one of the most potent agents for elevating serum cholesterol level. Labels that read "made with vegetable oil" give an erroneous implication that the product is to be preferred over one containing dairy fat.

Baked Goods

c. Reduction of saturated fat, cholesterol and calorie content of baked goods. As the National Diet-Heart Study demonstrated, nutritionally excellent baked goods of all types can be prepared commercially in completely acceptable forms with reduced saturated fat, cholesterol and calorie content. Widespread marketing of these fat modified products should be encouraged.

Fats and Oils

d. Promotion of fats and oils low in saturated fats and cholesterol for table spreads, shortenings, cooking and salad dressings, etc. In some areas of the country, state and/or local laws prohibit the use of butter substitutes in restaurants and institutions. These laws should be repealed.

Egg Yolks

e. Reduction of egg yolk consumption. The yolk of the egg is the single highest source of cholesterol in the average American diet, as well as a source of considerable saturated fat. Ingestion of two eggs a day—in visible and/or invisible form (i.e., in prepared foods)—will seriously hamper dietary programs aimed at reducing serum cholesterol. Consequently the public should be encouraged to avoid egg yolk consumption, and the food industry should be persuaded to minimize

egg yolk content of commercially prepared foods. Food manufacturers have recently developed low cholesterol and low saturated fat egg substitutes which may be used successfully in quantity cookery and for scrambled eggs, omelettes, etc. Such developments should be encouraged.

Food Labeling

f. Modernization of regulations on labeling and definition of foods. In December 1959 the Food and Drug Administration introduced into the Federal Register the statement: "The role of cholesterol in heart and artery diseases has not been established. Consequently, it ruled that advertising claiming that the consumption of a food product might protect against diseases of the heart and arteries was false and misleading. The Federal Register in May, 1965 published a proposal favorable to the labeling of edible fats. This was supported by the American Heart Association and the American Diabetes Association. In February 1966, however, the FDA rejected the recommendation to label edible fats and oils, but endorsed a study of this problem to be conducted by the Council on Foods and Nutrition of the American Medical Association. The Council completed its report and transmitted it to the FDA. The report favored such labeling but the FDA took no action.

The FDA's regulation with respect to labeling of foods should be reviewed and updated. A new approach to labeling is needed—to allow the consumer easily to identify nutrient content (particularly the amount and type of fat and cholesterol) in all foods, including commercially prepared mixed dishes, and to encourage the manufacture of nutritious products low in saturated fats and cholesterol.

Correspondingly rules and regulations of the USDA, state and local agencies on foodstuff definition, adulteration, etc., should be modernized to permit and encourage production, advertising and sale of products low in saturated fats and cholesterol (e.g., processed meats), made with moderate amounts of unsaturated oils instead of large amounts of saturated fats.

Government Programs

g. Improvement in school lunch, food stamp, other supplementary food programs and government administered nutrition practices (e.g., Armed Forces, Veterans Administration facilities). Policies, regulations, practices and educational aspects of these programs should be revised to encourage improved eating habits including consumption of low saturated fat, low cholesterol diets among children, teenagers, young adults and low income groups.

Public and Professional Education

h. Development of a comprehensive and sustained public and professional nutrition education program. To effect the required changes in dietary habits, it is essential that the entire community be actively involved through a comprehensive and sustained public and professional education program. This will deepen understanding and appreciation of the need for primary prevention and inform the public and health professions on ways of selecting and preparing foods consistent with sound nutritional practices.

Special emphasis must be directed toward developing effective instructional programs on nutrition in the educational curricula at all levels. For this purpose, particular attention should be given to the institution training health professionals with expertise in nutrition—e.g., college and university home economics departments, hospital dietitian instruction programs, schools of medicine, dentistry and nursing, and teachers' colleges. These sources should develop educational programs based on modern concepts of sound nutrition. Succeeding generations should have the advantage of this knowledge beginning in elementary school.

Food manufacturers have an excellent opportunity to provide public education through advertising. They should be encouraged to call attention in their advertising to the type and amount of fat and the cholesterol content of their products.

There is a great need for extensive and continuous dissemination by the news media of information on diet, as well as other risk factors. Public service communications, in this area should be substantially strengthened and broadened.

With proper education, information and the availability of fat modified foods, it will be possible for most Americans to make desirable changes in their diets without major dislocation of personal eating habits.

Americans should be encouraged to modify habits with regard to all five major sources of fat in the U.S. diet—meats, dairy products, baked goods, eggs, table and cooking fats. Specifically a superior pattern of nutrient intake can be achieved by altering habits along the following lines:

- Use lean cuts of beef, lamb, pork and veal, cooked to dispose of saturated fat and eaten in moderate portion sizes;

- Use lean meat of poultry and fish;

- Use fat-modified,² processed meat products (frankfurters, sausage, salami, etc.);

- Use organ meats (e.g., liver) and shellfish in moderation since they are higher in cholesterol than muscle of red meat, chicken and fish;

- Avoid fat cuts of meat, addition of saturated fat in cooking meat, large meat portions and processed meats high in saturated fat;

- Use low fat and fat modified dairy products;

- Avoid high saturated fat dairy products;

- Use fat modified baked goods (pies, cookies, cakes, sweet rolls, doughnuts, crullers);

- Avoid baked goods high in saturated fat and cholesterol;

- Use salad and cooking oils, new soft margarines and shortenings low in saturated fat;

- Avoid butter, margarine and shortenings high in saturated fat;

- Avoid candies high in saturated fat;

- Avoid egg yolk, bacon, lard, suet;

- Use grains, fruits, vegetables, legumes.

² Throughout this set of guidelines *fat modified* refers to products made with reduced saturated fat and cholesterol content.

C. PREVENTION OF CORONARY HEART DISEASE

(Report of a Joint Working Party of the Royal College of Physicians of London and the British Cardiac Society)

1. SUMMARY AND RECOMMENDATIONS

1.1 *Introduction*

1. The aim of this Working Party has been to formulate the best possible advice that can at present be given to medical practitioners towards the prevention of coronary heart disease (CHD).

2. There is considerable evidence that the causes of CHD are largely environmental and are rooted in the modern, affluent way of life. CHD risk factors such as cigarette smoking, physical inactivity, obesity and plasma lipid concentrations reflect aspects of our social behaviour. This report is particularly concerned with those risk factors that can be modified.

3. The risk of CHD varies according to the total burden of risk factors present and the recommendations emphasise this multifactorial concept of risk. When dealing with an individual, the overall degree of CHD risk must be considered rather than deciding whether any particular factor has reached a "critical" level requiring treatment.

4. The measures recommended carry the reasonable hope of conferring some benefit to the community and none of them has a cost that approaches the cost of inaction.

1.2 *Diet*

1. Dietary recommendations for the whole community involve a reduction in the amount of saturated fats and partial substitution by polyunsaturated fats.

2. Where plasma lipid concentrations indicate particularly high risk or where other risk factors are concurrently present, the dietary recommendations should be followed more strictly.

3. Widespread screening for plasma lipid levels is not recommended but estimations should be carried out in certain groups known to be at high risk for CHD.

4. Maintenance of a desirable weight is important as obesity is commonly associated with other more potent risk factors for CHD. Weight reduction should be based on a decrease in all the dietary components; sugar and alcohol are recognised as common sources of excess energy intake. A combination of exercise and diet is strongly recommended.

1.3 *Smoking*

1. Every effort should be made to discourage cigarette smoking, particularly in the young. Doctors and other health workers should set an example.

2. Less harmful methods of smoking should be advised for those who are unwilling to stop.

1.4 *Blood pressure*

1. Blood pressure should be recorded for every patient, using the opportunities provided by any consultation.

2. In those with even moderately raised blood pressures, the control of other risk factors (cigarette smoking, diet, physical inactivity) is important.

3. Treatment of raised blood pressure is at present justified on the grounds of reducing the risk of stroke and other implications. Its effect on CHD risk is not yet established.

1.5 *Physical activity*

1. Physical activity should be encouraged at all ages in both men and women.

2. Few need to consult their doctor before making a graded increase in their physical activity.

1.6 *Stress*

1. While acute stress may occasionally precipitate a heart attack, it is difficult to prove that chronic stress contributes to the development of CHD.

2. The management of stress, whether it be domestic or occupational in origin, is a normal part of medical practice.

3. Initiative, diligence, leadership and hard work, especially in young people, should not be discouraged on the mistaken supposition that these qualities are indicators of future CHD.

1.7 *Diabetes Mellitus*

1. Reversal of risk factors for CHD should form part of the care of diabetics.

2. Dietary policy for individual diabetics should be determined as much by their plasma lipid concentrations as by the blood sugar response.

1.8 *Oral contraceptives*

1. Oral contraceptives constitute a negligible risk in women under the age of 40 years who do not have any risk factors for CHD.

2. They should be used with caution in women over 40 years, those with a family history of premature CHD, and in women who are heavy cigarette-smokers (more than 20 a day) or have other risk factors.

1.9 *Children*

1. Measures recommended to prevent the development of CHD apply to children as well as to adults since all of the major risk factors found in adult life can occur during childhood. All those concerned with the care of children should be active in the prevention and management of these factors.

1.10 *General practice*

1. General practice should provide the main means of identifying those at high risk of CHD.

2. Mass screening for CHD and its associated risk factors is not recommended.

3. The efforts of general practitioners should be supported by a general health education policy that involves hospital and community physicians and their supporting staff.

4. Selective health examinations should be carried out in those groups known to be at high risk for CHD.

5. Interested general practitioners should be encouraged to extend health examinations to other groups of patients where this can be done by the use of existing facilities and services.

1.11 Wider implications of the recommendations

1. It was not the purpose of the Working Party to consider the implications of their recommendations for research or for government. However, attention is drawn briefly to areas that may deserve further consideration by other bodies. In the overall allocation of resources the Working Party considered that the achievements of acute coronary care, coronary ambulances and coronary artery surgery could not bring about a major reduction in the overall burden of heart disease in the community. This must come from preventive measures.

2. *Education*.—To bring about the recommended changes in behaviour relating to diet, physical activity and cigarette smoking will require the sustained involvement of the community at all levels, aimed particularly at the young. A comprehensive public and professional educational programme will be needed, together with the involvement and co-operation of food manufacturers, educational authorities and the mass media. Apart from formal health education, much can be done by medical practitioners and other health workers who understand the problem and are prepared to provide positive advice to individuals and the community regarding the risk factors for CHD.

3. *Smoking*.—The reduction of cigarette smoking will require fiscal measures by the government and the control of advertising. These measures may be at least as effective as general health education and possibly more so.

4. *Diet*.—There are considerable implications in the dietary recommendations for national food policy, for the producers and the manufacturers of food and for the regulations concerning food labeling. Nutritional practices and catering in schools, hospitals, the Armed Forces and other organisations may require to be reviewed.

5. *Physical activity*.—Any improvement in patterns of physical activity can come only from leisure time pursuits. Adequate and convenient recreational facilities are required if the recommendations made are to be effective.

2. INTRODUCTION

2.1

This is the third of the Working Parties set up jointly by the Royal College of Physicians of London and the British Cardiac Society to consider various aspects of coronary heart disease (CHD). The aim of this Working Party has been to formulate the best possible advice that can at present be given to medical practitioners towards the prevention of CHD: i.e. myocardial infarction, angina pectoris and sudden death. The report is intended for general practitioners and for hospital and

community physicians. It is hoped that it will also be of value to nurses, paramedical personnel and community health workers.

2.2

The Working Party set out to evaluate critically the available information and to give brief and clear advice, indicating those areas of knowledge that remain controversial. While conscious of the need to provide useful guidelines for present action and aware of the lack of conclusive evidence on which some of its recommendations would be based, the Working Party considers that the recommendations represent a reasonable approach to the prevention of CHD.

2.3 *The concept of risk*

The term "risk factor" is widely used to describe those characteristics found in healthy individuals that relate to the subsequent appearance of CHD. The term is useful to the physician in helping him to consider his patients' future CHD risk and to think of preventive action rather than in conventional therapeutic terms only. It is clear that the risk of CHD is determined by the aggregate of individual risk characteristics. The vast differences in the frequency of CHD between populations and in the risks between individuals within populations can largely be explained by the presence of these factors.

A risk factor may be associated only with risk of disease in the future and some would prefer to use "risk indicator," reserving the term "risk factor" for those characteristics considered from other evidence to be causal. However, the term "risk factor" is widely accepted and is used throughout this report in the knowledge that some such risk factors may not be causal. Knowledge of risk factors can be used in two distinct ways. Some factors identify the individual with high-risk status but are not modifiable, such as age, sex, and family history, or are questionably modifiable, such as personality. Other factors, such as cigarette smoking or physical inactivity, identify the need for action and also constitute the basis for intervention. This report is concerned in particular with those risk factors that can be modified.

2.4

Primary prevention refers to attempts at preventing a first manifestation of CHD. Secondary prevention refers to attempts at preventing recurrences in those who have survived a myocardial infarction or other manifestation of CHD. This report makes no distinction between primary and secondary prevention in its recommendations since the boundary between these two aspects is often indistinct.

2.5 *Preventive trials*

Many preventive trials have been established in the past fifteen years in attempts to determine whether the incidence of CHD in individuals and in populations at apparently high risk could be lowered by direct intervention on the risk factors. These trials have been either primary or secondary in nature or a mixture of both. The aim of the primary prevention trials has been to diminish the appearance of new cases of CHD in the community; the aim of the secondary prevention is to

prevent the recurrence of events in those who have already manifest CHD. Preventive trials are costly and require that a large number of people be followed for many years. They can be done well only by a trained team including clinicians, epidemiologists, statisticians, nurses, technicians and dietitians, to mention only some of those involved. They may be unifactorial, in which only one factor is modified, e.g. diet or smoking, or multifactorial, in which an attempt is made to control a number of risk factors. The results of preventive trials to date have recently been critically reviewed (Blackburn, 1974, Fejfar, 1975) and, in spite of encouraging trends, conclusive evidence of the effectiveness of any particular regime has not emerged. On the other hand, we do not consider these results should be discounted.

Many trials, mainly multifactorial, are still in progress and in due course their results may indicate the degree of acceptance of health education in free-living populations and the effect of this education on the incidence of CHD.

2.6 Present approach

This Working Party has tried to steer a course between the academic and the pragmatic views of CHD prevention, between the nihilism of those awaiting final scientific proof before taking action and the enthusiasm of those determined to eliminate every risk factor from all individuals. We consider that the present size of the CHD problem in this country and the small effect of medical and surgical treatment on the mortality rate from CHD justify attempts to prevent the disease we cannot cure. Research and controlled trials must continue but it now seems an appropriate time for energetic action based on a balance of probabilities. The measures we recommend have a reasonable hope of conferring some benefits, and none of them has a cost that approaches the cost of inaction. The degree of energy with which these measures should be applied must depend on the risk in the individual and on the choices the individual decides to make. His ability to make decisions regarding his life pattern and the risk of future disease will depend on his understanding of the concept of risk. This will require considerable effort in health education, and certainly the knowledge that a positive family history, sedentary living, obesity and cigarette smoking are risk factors of importance should be widely disseminated. We are convinced that the major impact of preventive measures should come through contact between patient and general practitioner and that this should be supported by a general health education policy that involves hospital and community physicians and their supporting staff.

3. CORONARY HEART DISEASE IN THE UNITED KINGDOM

3.1

In the United Kingdom, coronary heart disease (CHD) is the major cause of death in middle and old age and this section provides some basic information regarding the nature of the problem. Some information is also provided for the Republic of Ireland.

3.2 CHD as a cause of death in middle-aged men and women¹

In men aged 45 to 54 years (Fig. 1) 52 percent of all deaths in 1973 were due to cardiovascular disease (CVD) and more than three-quarters of these deaths were due to CHD. Almost half of the remaining CVD deaths were due to stroke. This can be compared with 26 percent of deaths caused by cancers and 7 percent by accidents, poisoning or violence. In women in the same age group, 28 percent of deaths were cardiovascular; less than half of these were due to CHD and slightly less than one-third to stroke. Even in the men 35 to 44 years of age CVD comprised 41 per cent of all deaths and, again, almost three-quarters of these were due to CHD.

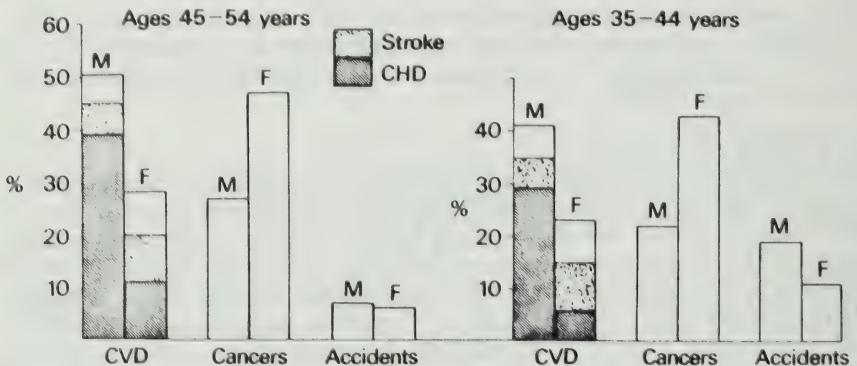


FIGURE 1.—Causes of death in men and women aged 45 to 54 years and 35 to 44 years, in England and Wales 1973.

3.3

The annual death rates per 100,000 population of men and women in three age groups are shown for England and Wales, Scotland, Northern Ireland and the Republic of Ireland (Figs. 2 and 3, and Table 1). In each country and in all three age groups between 1950 and 1972 there was a steady increase in the death rate from CHD in men. During this period the death rate in the younger men (35 to 44 years) increased much more rapidly than that of the older men (Table 1). In men in the two older age groups (45 to 54 and 55 to 64 years), there appears to be a further increase in 1973.

¹ Most of the data is derived from the Registrar General's Statistical Reviews (H.M.S.O.) and the same criteria have been adopted for CHD as in the DHSS Report on Diet and Coronary Heart Disease (1974). The International Classification of Diseases (ICD), 6th and 7th Revisions, classifies CHD in Categories 420-422 and these are used for data from 1950 to 1967. From 1968 onwards the 8th ICD Revision in which CHD corresponds with Categories 410-414 is used.

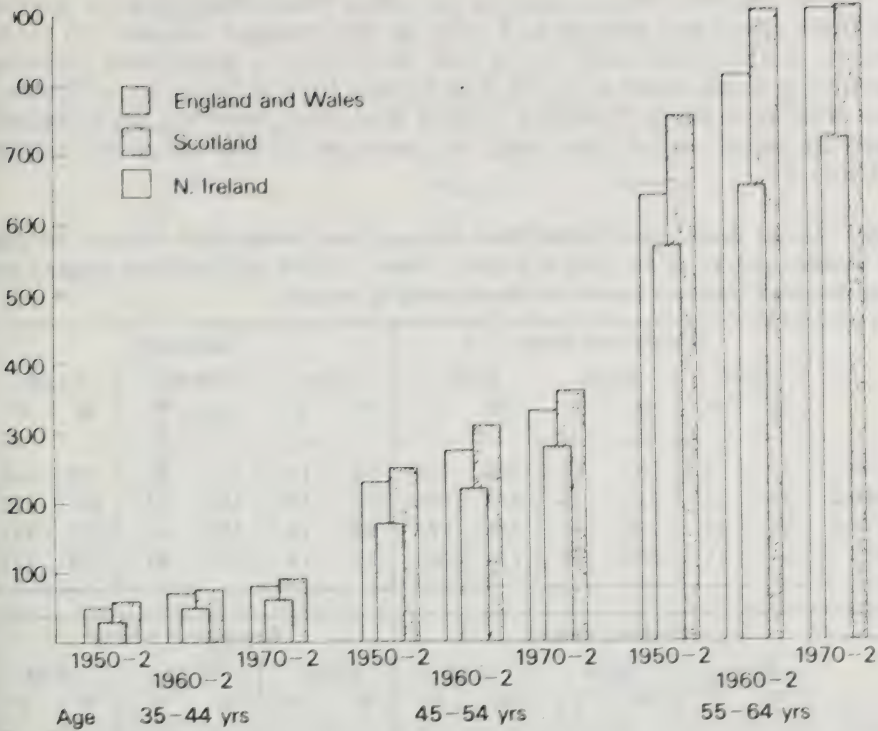


FIGURE 2.—Annual death rate from coronary heart disease (ICD 410-414) for men aged 35 to 64 years in 1950-1952, 1960-1962 and 1970-1972 in England and Wales, Scotland and Northern Ireland. (Rates per 100,000.)



FIGURE 3.—Annual death rate from coronary heart disease (ICD 410-414) for women aged 35 to 64 years in 1950-1952, 1960-1962 and 1970-1972 in England and Wales, Scotland and Northern Ireland. (Rates per 100,000.)

There has been little change in the death rates from CHD in women in these three age groups and only in the younger women (35 to 44 years) in England and Wales has there been a significant increase occurring since about 1958-60. The figures for the Republic of Ireland are similar to those from the United Kingdom, showing an increased rate in middle-aged men and no increase in the rates in women (Table 1).

Table 1. Annual death rates/100,000 from coronary heart disease (ICD 410-414) for men and women aged 35 to 64 years in 1950-2, 1960-2, 1970-2 and 1973 for England and Wales, Scotland, Northern Ireland and the Republic of Ireland.

	England and Wales						Scotland					
	35-44		45-54		55-64		35-44		45-54		55-65	
	M	F	M	F	M	F	M	F	M	F	M	F
1950-2	33	8	167	42	566	211	53	18	248	74	755	334
1960-2	53	8	217	39	655	194	75	14	313	73	891	327
1970-2	66	10	274	46	717	194	88	19	355	85	915	317
1973	64	11	286	52	731	205	87	15	373	91	968	331

	Northern Ireland						Republic of Ireland					
	35-44		45-54		55-64		35-44		45-54		55-64	
	M	F	M	F	M	F	M	F	M	F	M	F
1950-2	50	18	230	79	634	301	39	26	173	90	507	330
1960-2	72	14	272	74	810	287	53	19	192	71	564	253
1970-2	80	14	331	67	906	296	58	13	247	71	692	265
1973	70	21	362	60	867	329	62	9	294	70	726	263

3.4 Regional variations in mortality

For men and women in all three age groups the death rates from CHD are higher in Scotland and Northern Ireland than they are in England and Wales or the Republic of Ireland (Figs. 2 and 3). Even within each country there is considerable geographic variation. In England and Wales there is a ratio of about 2:1 between the highest and the lowest rates for CHD and for cerebrovascular disease, with a tendency for the mortality rates to be low in the South-East of England and high to the North and to the West. Within Britain there is no consistent urban: rural difference in CHD mortality.

3.5 Sex and age

The number of hospital admissions rises to a peak in middle-aged men but age-specific incidence and mortality rates rise more or less logarithmically throughout life, approximately doubling for every 10 years of advancing age. The male:female ratio diminishes progressively from a maximum of around 6:1 under 40 years to about equality in the very elderly (Fig. 4).

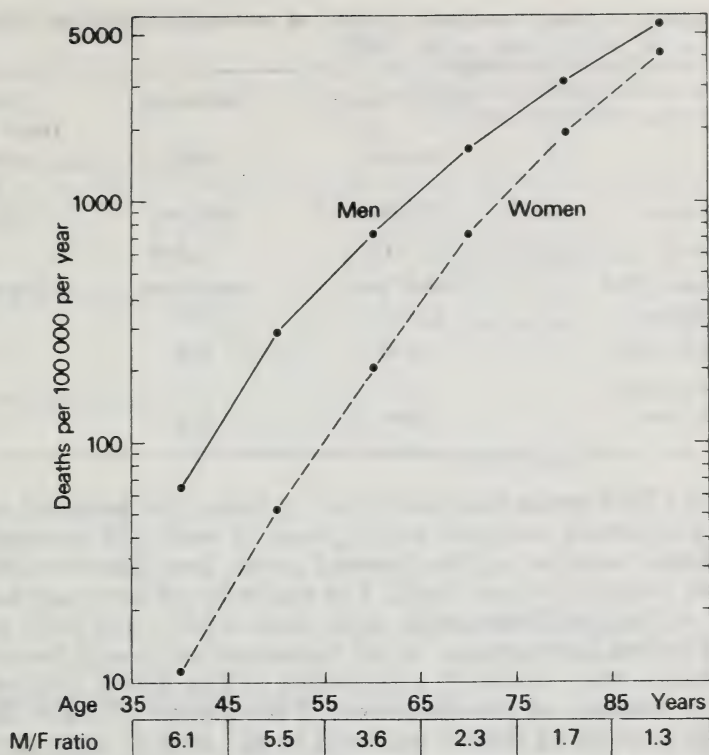


FIGURE 4.—Mortality rates/100,000 from coronary heart disease (ICD 410–414) for men and women by age in England and Wales 1973 and male/female mortality ratios.

3.6 Coronary heart disease in the community

1. Hospital admissions give a limited view of the problem of CHD. A more accurate picture comes from community studies of myocardial infarction and sudden death in Oxford, Edinburgh, and London (Tower Hamlets). The results of these studies show many similarities and some differences (Table 2). The attack rate includes both first and recurrent attacks and in 50 percent of events the subject had a previous history of angina or infarction.

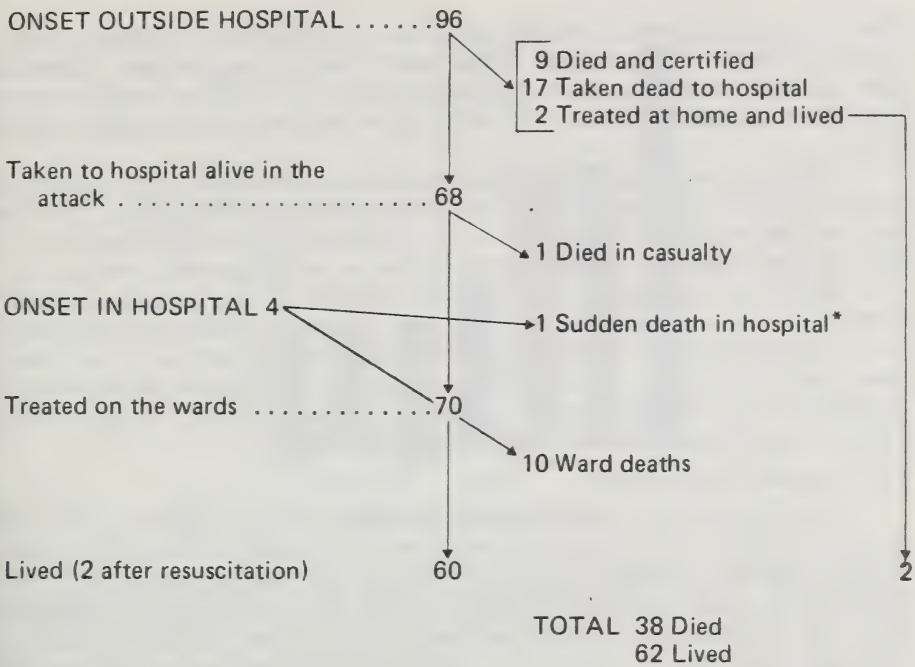
Table 2. Findings in three community studies of myocardial infarction (Kinlen, 1973; Armstrong *et al.*, 1972; Pedoe *et al.*, 1975).

	Oxford region 1966-67	Edinburgh 1967	London Tower Hamlets 1970-72
Total population	325,000	500,000	165,000
Cases registered	373	1,858	1,039
Attack rate per 1,000 men per annum	(40-69 yrs) 6	(40-69 yrs) 16	(45-64 yrs) 10
28-day fatality rate	59%	33%	40%
Deaths in hospital as fraction of total	28%	27%	32%

2. Most CHD events had their onset at home (64 percent) and only a small proportion occurred at the place of work (13 percent). Most of the deaths occurred at the place of onset; less than one-third were moved to hospital before death. The majority of coronary deaths occurring within the first month took place within one hour and most within the first few minutes. In all three studies, nearly two-thirds of fatal attacks were medically unattended before death. Figure 5 illustrates the outcome of attacks in one of the studies (Tower Hamlets). Nearly 40 percent of deaths occurred in the first 28 days and at the end of one year 45 percent of men and 50 percent of women were dead.

3. In the London study, half the survivors reached hospital about four hours after the onset of acute symptoms, by which time 70 percent of all deaths had already occurred. Even if it had been possible to reduce the delay to one hour, 60 percent of deaths would already have taken place. It would seem that the potential benefit from improving emergency services would be disappointingly small.

4. Most deaths from CHD occur far too suddenly for present forms of medical attention to be effective, and in many other cases irremediable myocardial injury may cause lasting disability from angina and dyspnoea. Coronary ambulances, intensive care and other therapeutic services have saved individual lives but they cannot hope to achieve a major reduction in the overall burden of CHD in the community. This must come from preventive measures.



* Patients found dead who were admitted for other causes e.g. elective surgery.

FIG. 5.—Disposal and fate of 100 male coronary heart attack victims between onset and 28 days. (Based on 707 cases in Tower Hamlets).

4. PLASMA LIPIDS

4.1 Introduction

1. The plasma lipids we are particularly concerned with in this section are cholesterol and triglycerides. The term hyperlipidaemia means an elevation of either of these to the levels that prospective studies within communities have shown to be associated with an increased risk of CHD. The actual levels, of course, differ in different communities and because the risk of CHD in relation to plasma lipids is a graded phenomenon, no precise “cut-off” points can be defined. Where levels are indicated later in this section, they represent guide lines only. Plasma is referred to throughout this report, but serum gives an almost identical result. There are many different systems used for classification of the plasma lipids and Appendix 1 provides more detailed information.

2. The plasma contains the lipids that pass across the intima of the arterial wall. It contains only 10 to 15 percent of the total body cholesterol and is a poor indicator of total body lipids. However, all the available information regarding lipids and the risk of CHD relates to plasma concentrations, and the significance of total body lipids to vascular disease is not known.

3. Plasma lipid levels are influenced by the endogenous rates of synthesis and excretion and by genetic, dietary and other factors. Obesity, alcohol, oral contraceptive drugs, and physical inactivity can increase plasma lipid levels.

4. A single lipid estimation should be interpreted with great caution as many other factors might influence plasma levels. These include

recent weight change, a recent myocardial infarction, seasonal variations and even the position of the body during venesection; there is also a large random within-subject variability. It is advisable to repeat the estimation before committing a subject to long-term treatment.

5. Different methods used in different laboratories may give differing results on the same specimen. Even within the same laboratory, results may not be readily comparable over a period of time. Wherever possible, it is advisable to continue using the same laboratory service.

6. Blood for estimation of plasma cholesterol can be taken at any time of the day and the subject need not be fasting. Tourniquets should be briefly applied. For estimation of plasma triglycerides, blood samples should be taken after a 12 to 14 hour fast to minimise the contribution from dietary sources; alcohol taken during the preceding 24 hours may increase the plasma triglycerides.

4.2 Plasma cholesterol

1. Population studies comparing communities in different parts of the world have shown a strong positive relationship between the mean level of plasma cholesterol in a community and the incidence of CHD. In addition, the community cholesterol level is positively correlated with the percentage of total calories derived from saturated fats in the diet. (Appendix 2 provides detailed information on the nature of dietary fats.) Communities with low mean concentrations of plasma cholesterol in middle-aged men, e.g. 150–200 mg/dl (3.9–5.2 mmol/litre) have a low risk of CHD. Viewed from this international perspective the average plasma lipid levels in the United Kingdom indicate that we are a community at a considerable risk of CHD.

2. Within several of the developed countries the plasma cholesterol concentration in individuals is a major predictor of CHD. Prospective studies carried out within defined communities have shown that the risk of developing CHD increases with increasing concentration of plasma cholesterol (Fig. 6). The gradient of CHD risk seen in this American series will not be exactly the same in other countries. However, prospective studies in the United Kingdom have shown a similar relationship between plasma cholesterol concentration and the risk of CHD. In the London busmen study, those in the highest quarter of the plasma cholesterol distribution had CHD rates four times those in the lowest quarter.

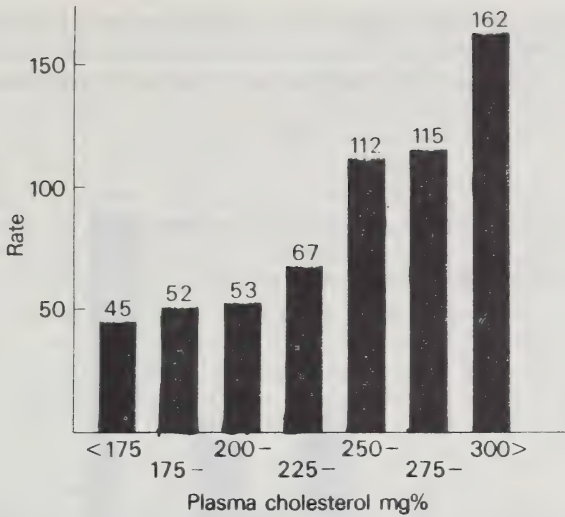


FIGURE 6.—Plasma cholesterol and first major CHD events (including non-fatal myocardial infarction, fatal myocardial infarction and sudden death due to CHD). Ten-year rates per 1,000 men aged 30 to 59 years at entry. U.S.A. National Cooperative Pooling Project (Stamler and Epstein, 1972).

3. The many individuals in the community with moderate elevations of plasma cholesterol contribute more CHD events than the few subjects with severe hyperlipidaemia. This is because there are many more people with moderate elevations and moderate risk of CHD than there are with very high levels and high risk of CHD. Although the incidence of CHD is particularly high in individuals with familial hypercholesterolaemia, this group makes a very small contribution to the overall incidence of CHD in the community. In these families, CHD occurs prematurely.

4.3 Plasma triglycerides

1. We are here concerned with the endogenous triglycerides that are evident in fasting subjects and not the exogenous forms that are related to recent food or alcohol intake.

2. In communities with a moderate to high incidence of CHD, the plasma triglyceride level is an additional risk factor. Its effect is weaker than that of the plasma cholesterol and may be due at least in part to the increase in plasma cholesterol that occurs with the increase in the total concentration of the triglyceride-rich very low density lipoproteins (VLDL) in the plasma (*see* Appendix 1).

3. Hypertriglyceridaemia is not usually found before the third decade.

4.4 Relation of plasma lipids to other risk factors

1. The risk of developing CHD in association with hypercholesterolaemia is considerably enhanced by the presence of hypertension, cigarette smoking and diabetes mellitus (Fig. 7). This figure illustrates the effects of various combinations of risk factors when a single cutting point is used to separate "high" plasma cholesterol concentrations from those which are "not high". This arbitrary and somewhat undesirable approach is used only to convey information about the synergistic ef-

fects of the various risk factors. In the same way, blood pressure is separated into "hypertension" and those who do not have "hypertension", and cigarette smoking implies any use of cigarettes at entry into the study.

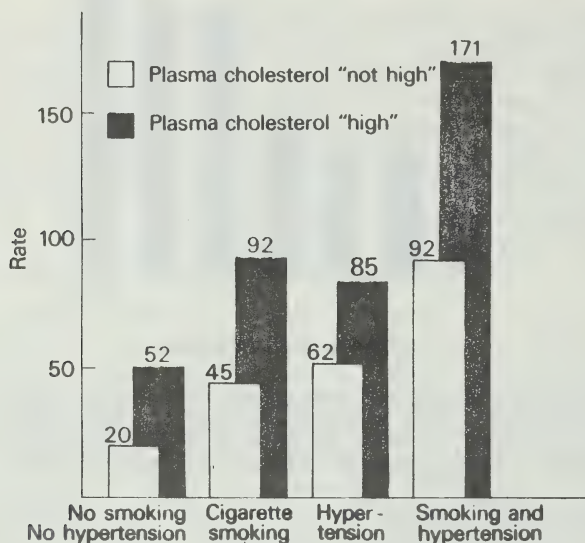


FIGURE 7.—Combined effects of plasma cholesterol, cigarette smoking and hypertension on the risk of CHD. Ten-year rates per 1,000 for first major CHD events in men aged 30 to 59 years at entry. U.S.A. National Cooperative Pooling Project (Stamler and Epstein, 1972).

4.5 Reversal of hyperlipidaemia

Plasma lipid levels can be lowered in healthy subjects with moderately raised levels of plasma cholesterol and in most forms of hyperlipidaemia by an appropriate diet, either alone or in combination with drugs. For the usual (average) levels of plasma lipids in our community, simple (but specific) dietary recommendations may be sufficient; for the more severe forms of hyperlipidaemia the regime may have to be more strict. Reductions in plasma lipid concentrations can be achieved in the majority of subjects, although after a time there may be some return towards the previous levels, mainly as a result of inattention to the recommended diet. In familial hypercholesterolaemia it may prove impossible to achieve normal (desirable) plasma cholesterol concentrations despite assiduous attention to treatment.

4.6 Results of lowering plasma lipids

1. Most attempts at prevention of CHD through the lowering of plasma cholesterol have been based on modifications to the diet.

2. Studies in familial hypercholesterolaemia with xanthomata, although not strictly controlled, suggest that diets low in saturated and high in polyunsaturated fats may lower the high incidence of CHD in this group.

3. Trials of the effects of changing diet on the prevention of CHD have not been wholly satisfactory. Both of the major trials designed to

prevent CHD have serious defects although it is of interest that they both showed a similar favourable trend. Since most existing trials are concerned with the concurrent management of other factors (smoking, blood pressure, physical activity, etc.) in addition to diet, it is unlikely that clear evidence regarding the effect of altering a single factor such as hyperlipidaemia will emerge.

Los Angeles Veterans Administration Study (1959-67). This American trial is probably the best so far in this difficult field but it is a mixed primary and secondary prevention study involving men over 55 years (average age 65 years) living in an institution. The groups, properly randomised, ate in different canteens. The experimental group was given a diet low in saturated fats and rich in polyunsaturated fats and the control group received the ordinary American diet. There were fewer CHD events in the diet group but not a statistically significant level. If other end-points such as stroke were included, a significant difference was observed in favour of the diet group. There was, however, no difference between the groups in total mortality.

Finnish Mental Hospitals Study (1958-71). This trial was also a mixed primary and secondary study involving men and women, average age 51 years, living in two mental hospitals. The experimental diet was proportionately lower in saturated fats and higher in polyunsaturated fats with no great reduction in total fat content. Each hospital used either the experimental or the usual Finnish diet for a six-year period and then changed to the other diet. The population changed considerably during the course of the trial. During the period on the experimental diet, the men in each hospital experienced approximately half the mortality rate of CHD compared with the control period on the usual Finnish diet. Women showed the same trend but it was smaller.

4.7 *Conclusion*

It is not surprising that attempts to lower plasma lipids by relatively small amounts in middle-aged or elderly populations have had no dramatic effects on the incidence of CHD. Maximum benefit might be possible only if appreciable reductions in plasma lipid levels were life long. It seems unlikely that conclusive evidence of a particular dietary regime reducing the incidence of CHD will be provided in the foreseeable future. However, there is probably sufficient evidence regarding the role of diet and blood lipids in CHD to make dietary recommendations in the hope of affecting a degree of prevention, particularly as these recommendations have no known adverse effects on health.

4.8 *Recommendations*

1. We consider that widespread population screening for plasma lipid levels is not justified. We already know the pattern of plasma cholesterol levels in our adult population and we know these levels indicate that we are a population generally at risk for CHD. It would neither be practical nor feasible to measure plasma lipid levels in the entire population. There are, however, certain groups in which plasma lipid estimations should be carried out—

- (a) Subjects with a strong family history of premature CHD.
- (b) Siblings and children of patients with CHD, particularly where it has occurred in individuals under 55 years of age or where patients

have been found to have high plasma cholesterol of levels, in the region of 275–300 mg/dl (7.1–7.8 mmol/litre) or above.

(c) Siblings and children of subjects with familial hypercholesterolaemia.

(d) Subjects in whom several risk factors are found to be concurrently present, e.g. hypertension, cigarette smoking, obesity, diabetes mellitus.

2. As we are recommending plasma lipid measurement in selected subjects only, we suggest that both plasma cholesterol and plasma triglycerides be measured in the fasting state on the initial occasion.

3. The focus for lowering plasma cholesterol levels and controlling hyperlipidaemia should be in the middle years (30 to 50 years) where the risk of CHD is most enhanced by raised lipid levels. We recommend that no attention should be paid to plasma lipid levels in healthy subjects over 60 years of age.

4. The need to lower plasma lipid concentrations becomes greater as the levels increase but it is difficult to define fixed "cut-off" points for particular decisions on management. When dealing with an individual, the overall degree of CHD risk must be considered, taking into account all the risk factors present, rather than deciding whether a lipid estimation falls above or below a particular level. In this report, levels have been provided with some reluctance, in order to give guidance to practitioners; it would be meaningless to give no figures at all. Moderate elevations of plasma lipids, that might otherwise be regarded as "acceptable" becomes more important in terms of intervention where several risk factors are concurrently present, e.g., cigarette smoking and hypertension.

5. It is advisable to lower plasma cholesterol concentrations that are in the region of 275 to 300 mg/dl (7.1–7.8 mmol/litre) or above bearing in mind the known risk of a first major CHD event in such subjects. Similarly, it would seem desirable to lower the plasma cholesterol concentration when it lies in the region of 250 mg/dl (6.5 mmol/litre) or above particularly if other risk factors such as hypertension, cigarette smoking or physical inactivity are concurrently present. It is advisable that fasting plasma triglyceride levels in the region of 175 to 200 mg/dl (2.0–2.3 mmol/litre) should be regarded as hypertriglyceridaemia. The finding of such levels emphasises the need to control obesity by dietary means.

6. Dietary fat is one of the main determinants of the average plasma cholesterol in a community and the levels can to an extent be related to the quantity and proportion of saturated and polyunsaturated fats in the diet. We therefore make general dietary recommendations that we regard as applicable to the whole community, and specific dietary recommendations directed to the control of marked elevations of plasma cholesterol or plasma triglyceride levels, i.e. hyperlipidaemia. The general and the specific sets of recommendations are similar in nature but differ in degree.

For the purposes of this document and in order to provide some guide lines, we regard a plasma cholesterol concentration in the region of 275 to 300 mg/dl (7.1–7.8 mmol/litre) or above and a plasma triglyceride concentration in the region of 175 to 200 mg/dl (2.0–2.3 mmol/litre) or above as hyperlipidaemia. It should not be assumed

that levels below those regarded as hyperlipidaemia are biologically normal, i.e. conducive to good health and freedom from CHD (see 4.2 and Fig. 6).

4.9 *Dietary recommendations for the community*

4.9.1 *General dietary recommendations*

These are made because of the current levels of plasma lipids in the United Kingdom, the known relationship between these levels and the risk of CHD, and because the major determinants of plasma lipid levels in the population are dietary. These recommendations are in general agreement with those previously made to the United Kingdom Government by the DHSS Committee on Medical Aspects of Food Policy (Diet and Coronary Heart Disease 1974). (Appendix 2 provides detailed information on the nature of dietary fats.)

(a) The amount of fat in the diet should be reduced from the present level of over 40 percent of total calories towards 35 percent of total calories.

(b) Reduction of fat intake should apply particularly to saturated fats, i.e. fats from animal sources or hardened (hydrogenated) fats of vegetable or marine origin.

(c) A reduction in saturated fat sufficient to produce a significant fall in plasma cholesterol level is likely to be unacceptable unless there is a measure of substitution by polyunsaturated fats. We have become accustomed to a diet rich in fat, and foods high in saturated fats contribute considerably to the average diet, e.g. butter and other dairy products, cooking fats, meat, cakes and pastries. Foods high in saturated fats should therefore be partially replaced by foods high in polyunsaturated fats; this will also contribute to the lowering of plasma cholesterol levels.

(d) A general reduction in total calorie intake is indicated in those who are obese. This may be partly achieved by reduction in total fat intake but may also require some reduction in carbohydrate intake. Sugar and alcohol are both common sources of excess calorie intake and those who are overweight should reduce their intake of these items.

What these Recommendations Mean to the Individual. The fat in our diet comes mainly from meat, dairy products, margarine, cooking fats and cakes/pastries. A small reduction in all these foods could lead to a considerable reduction in total fat intake. In order to reduce our total fat intake and particularly the saturated fats, there are a few simple recommendations for general usage—

(a) Eat less meat and fewer egg yolks; eat more poultry and fish. Choose lean meat and remove visible fat from meat. Grill rather than fry.

(b) Use butter sparingly; preferably use a soft margarine high in polyunsaturated fats. In general, avoid cream and the top of milk.

(c) Use oils rich in polyunsaturated fats for cooking, e.g. corn oil, sunflower oil, safflower oil. Avoid hard margarines or lard. Oils labelled merely "vegetable oil" may contain a good deal of saturated fat and very little polyunsaturated fat and should be avoided.

(d) Eat more vegetables and fruit of all kinds.

4.9.2 *Hypercholesterolaemia*

(a) Where plasma cholesterol levels are in the region of 275 to 300 mg/dl (7.1–7.8 mmol/litre) or above the general recommendations outlined above should be followed, but more strictly. In addition to the reduction in total fat and saturated fat intakes, a further reduction in dietary cholesterol may assist in the reduction of plasma cholesterol concentration.

(b) The effects of dietary modifications should be measured after three months and six months and then reviewed at intervals, perhaps annually.

(c) Failure of hypercholesterolaemia to respond to dietary management usually indicates lack of attention to the dietary recommendations. The advice of a dietitian would be of considerable help. Persistently high levels despite genuine adherence to the dietary recommendations indicates that drug treatment may be required.

What these Recommendations Mean to the Person with Hypercholesterolaemia

(a) Eat less meat; eat more poultry and fish. Choose lean meat and remove visible fat from meat. Grill rather than fry. Restrict meat meals to about eight a week.

(b) Use a soft margarine high in polyunsaturated fats instead of butter or other margarines, both for spreading and cooking.

(c) Use oils high in polyunsaturated fat for cooking, e.g. corn oil or sunflower oil. Avoid hard margarines or lard, or oils labelled simply "vegetable oil".

(d) Use skimmed milk; avoid cream.

(e) Eat no more than three eggs a week.

(f) Keep cheese intake down; use cottage cheeses.

(g) Restrict intake of cakes, pastries and biscuits unless they are made at home with suitable fats.

(h) Eat more vegetables and fruit of all kinds.

(i) It is the reduction in average fat intake over a period of time that matters. Exceptions can be made for special occasions.

4.9.3 *Hypertriglyceridaemia*

Fasting triglyceride concentrations in the region of 175 to 200 mg/dl (2.0–2.3 mmol/litre) or above are often associated with obesity and/or excessive alcohol intake and may occur in association with hypercholesterolaemia.

(a) Where hypertriglyceridaemia is associated with hypercholesterolaemia, the dietary recommendations under 4.9.2 should be followed. This usually results in a useful reduction in plasma triglyceride levels.

(b) Where hypertriglyceridaemia is the predominant finding, reduction of total calories is the most important dietary procedure and weight should be maintained at or near the ideal level. The advice of a dietitian may be helpful.

(c) To this end, there should be a reduction of carbohydrate, and of sugar in particular, and alcohol intake should be reduced to a low level (two small drinks a day).

4.10 Reminder

When dealing with an individual, it is the overall pattern of risk factors that must be considered, rather than deciding whether the concentration of plasma lipid falls above or below a particular level.

5. SMOKING

5.1

The risks that have been most emphasised for cigarette smokers are lung cancer and chronic bronchitis but, in fact, more than half of the excess mortality in smokers is due to cardiovascular disease. Expert committees in many countries have concluded that cigarette smoking is a major risk factor in coronary heart disease. In the United Kingdom about a quarter of the 40,000 deaths in men and women under 65 who die each year from CHD are considered to be closely associated with cigarette smoking.

5.2 Role as a risk factor

The evidence from several large studies shows that the risk for smokers of dying from CHD is about twice that of non-smokers. The risk is even greater among heavy smokers, i.e. those smoking more than 20 cigarettes daily (Fig. 8) and those who start before the age of 20. Death from CHD under the age of 45 years is unusual in a non-smoker. Among British doctors who smoked, the mortality from CHD was increased nearly 5 times at 35 to 44 years of age and nearly four times between 45 and 54 years. After 55 years of age the differences were much less. Some, but not all, studies show that heavy cigarette smoking increases the risk of sudden death. In one study, myocardial infarction occurred twice as frequently in heavy smokers than in non-smokers and sudden death five times more frequently (Fig. 9). The chance of developing a non-fatal myocardial infarction is also greater in cigarette smokers, and particularly in younger men and women who are heavy smokers. Smoking appears to be a much weaker risk factor for angina than for myocardial infarction. After smoking a cigarette, the walking capacity of a patient with angina is reduced. This effect is less marked with low nicotine cigarettes but still occurs even with nicotine-free cigarettes, probably due to the effects of carbon monoxide.

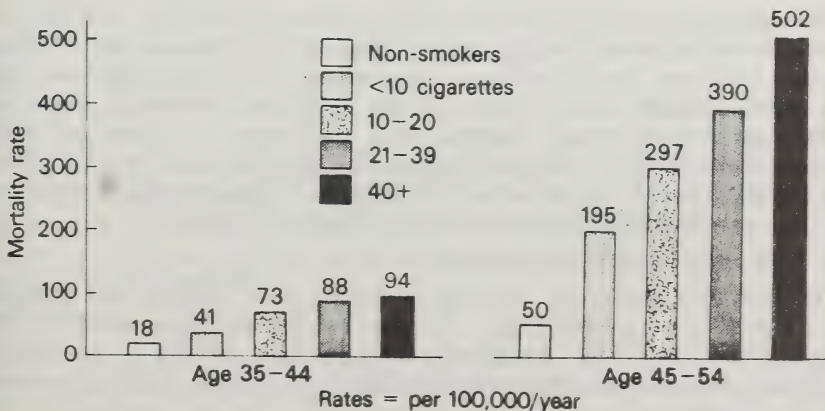


FIGURE 8.—Mortality rates for CHD in men by number of cigarettes smoked, in two age-groups (Kahn, 1966; Ball and Turner, 1974)

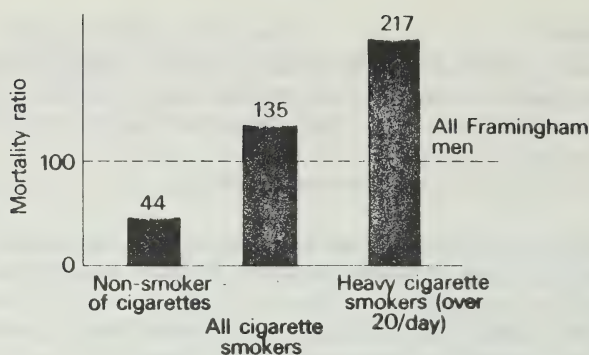


FIGURE 9.—Mortality ratios for sudden death in non-smokers, all smokers and heavy smokers (Stamler, 1968; Ball and Turner, 1974)

5.3 *Peripheral vascular disease, aortic aneurysm and stroke*

An even closer association has been found between cigarette smoking and peripheral vascular disease than with CHD, and almost all patients with intermittent claudication are smokers. Smoking a single cigarette will reduce calf blood flow and temperature in fingers and toes in healthy subjects and it will do so to a lesser degree in those with peripheral vascular disease. Atherosclerotic aortic aneurysm occurs much more frequently among cigarette smokers than non-smokers. The evidence of a relationship between cerebrovascular disease and cigarette smoking is less clear, although several studies show an increase in the mortality ratio for cigarette smokers.

5.4 *Coronary heart disease in women*

In England and Wales the mortality rate from CHD in women aged 35 to 44 years has apparently increased between 1958 and 1970. During the same period the average weekly cigarette consumption increased by 35 percent for all women in the United Kingdom and doubled in women aged 16 to 24 years. Several studies in the United Kingdom and Sweden have shown that women with myocardial infarction smoke much more heavily than healthy women. Women who smoke, and also use the contraceptive pill, appear to have an even greater risk.

5.5 *Pipes and cigars*

Most of the large prospective studies have shown the risk of CHD in smokers of pipes and cigars to be little greater than in non-smokers, but this may not apply to those who change from cigarettes to cigars or a pipe. Recent studies have shown that such smokers, especially those changing to small cigars, may continue to inhale, achieving carboxyhaemoglobin levels as high as in cigarette smokers. It is therefore possible that a major switch to pipe and cigar smoking might not result in a corresponding reduction in the risk of CHD.

5.6 *The constitutional hypothesis*

The strong association between smoking and CHD is not disputed but it has been suggested that it is coincidental and not causal. In this alternative view of the association, those who are likely to develop CHD are also constitutionally the kind of people likely to smoke

cigarettes. The hypothesis has been examined by a study of twins in Sweden but the numbers involved have been too small to allow any firm conclusion to be drawn. In any event, the constitutional hypothesis cannot readily account for the lower risk of CHD in ex-smokers. Familial and constitutional factors clearly affect the risk of death from CHD but no such factor has yet been found to account for the association between smoking and CHD. We consider the evidence indicates that cigarette smoking is an important cause of CHD.

5.7 *Summary*

The effect of smoking as a risk factor appears to be strongest for peripheral vascular disease and aortic aneurysm, followed, in diminishing order of relative risk by sudden death, myocardial infarction (especially in younger men who smoke heavily) and angina.

5.8 *Mechanisms*

The chief constituents of tobacco smoke thought to affect the heart are carbon monoxide and nicotine. Carbon monoxide in inhaled smoke leads to carboxyhaemoglobin levels of up to 10 or 15 percent, thus reducing the amount of oxygen available to the myocardium. Nicotine stimulates catecholamine secretion and thereby increases the work of the heart. Both carbon monoxide and nicotine may also, by different mechanisms, enhance atherosclerosis.

5.9 *Relation to other risk factors*

Smoking 20 cigarettes a day approximately doubles the risk of developing a coronary attack. Where no other risk factors are present the effect may appear small but when such factors as raised plasma cholesterol levels and high blood pressure are also present, the risk is greatly increased. (See Fig. 7).

5.10 *The reversibility of smoking*

The majority of teenagers who start smoking become established adult smokers. So great is the addiction that only about 15 percent of smokers stop before the age of 60. A concern for health is found to be the most important motive for stopping and the advice of their doctor is often effective in helping people to stop, especially during short illnesses. Simple, firm, unequivocal advice to stop smoking, given by a doctor to his patient, is as likely to be as effective as any other currently available anti-smoking measure. Where motivation is increased by a recent myocardial infarction, about 60 percent of patients can be persuaded by their doctor to stop for at least one year. No method is known to be more effective than this personal advice from doctor to patient, yet many patients have never been told by their doctor to stop smoking, even when they have CHD or chronic bronchitis. In recent years there has been a considerable reduction in the percentage of smokers in professional, executive and senior administrative groups, suggesting that when presented with the facts some people will stop smoking.

5.11 *The reversal of risk*

All reports show a reduction in the risk of developing a myocardial infarction or of death from CHD in those who stop smoking. A rapid fall of CHD mortality occurs within the first year, although in *may*

take ten years or more for the death rate of ex-smokers to reach that of non-smokers (Fig. 10). Even middle-aged men who have smoked heavily for many years appear to reduce their risk of a coronary event when they stop. Stopping smoking also helps to get rid of coughs and chest infections and to prevent the development of pulmonary heart disease. Angina may be improved. Patients with intermittent claudication who stop are much less likely to need amputation than those who continue to do so.

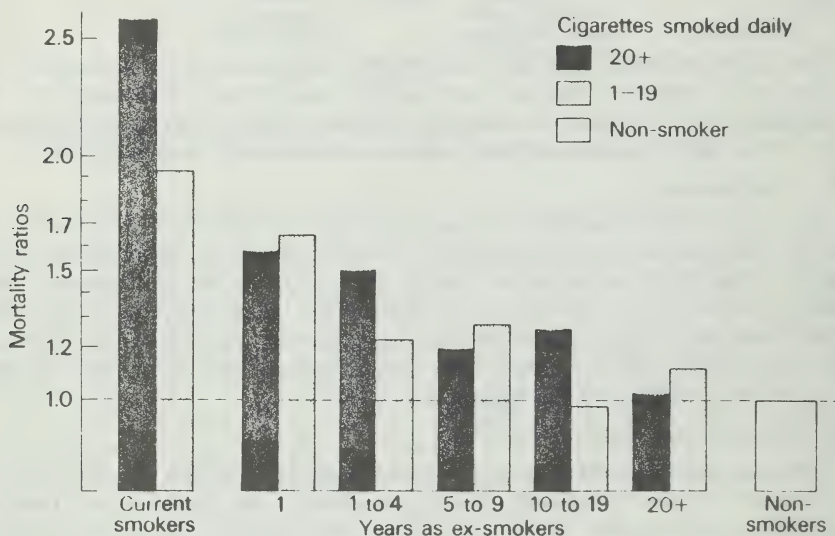


FIGURE 10.—Effect of stopping smoking on deaths from CHD in light and heavy smokers (Hammond and Garfinkel, 1969; Ball and Turner, 1974).

5.12 Recommendations

1. Every effort should be made to prevent cigarette smoking and to ensure that it is discontinued. The example of the non-smoking doctor is a major contribution to preventive health care. Non-smoking should be regarded as normal and smoking as abnormal behaviour.

2. Doctors should enquire about their patients' smoking habits and advise accordingly whenever the opportunity presents and whatever the reason for the visit.

3. The doctor's personal approach to his patient is the method most likely to succeed and a clear and relevant explanation of the dangers of smoking should be given to each patient. Most individuals need a defined plan leading to a complete break and continued support is necessary over the withdrawal period. Considerable patience may be required to persist with those who repeatedly fail in their attempts to stop smoking. Pamphlets with detailed advice on how to stop smoking are available from the Health Education Council, Action on Smoking and Health (ASH), and the Chest and Heart Association.

4. The aim should be a complete cessation of cigarette smoking. However, there is little point in continuing to press patients to stop if they clearly do not wish to do so. Not all subjects are able to stop smoking and less harmful methods should then be advised. These include—

- (a) Smoking less than five cigarettes a day.

- (b) Smoking filter cigarettes of progressively lower tar and nicotine content, using the Government Tar and Nicotine Table.

(c) Not inhaling. This is particularly important for cigarette smokers who change to cigars or pipes since they may continue to inhale and thus do not reduce their risk.

5. Particular care should be taken to advise children in families where one parent has had a coronary attack.

6. No drug has yet been found that consistently aids withdrawal. A placebo or tranquilisers may help some individuals over this period.

Addresses: Health Education Council, 78 New Oxford Street, London, WC1; Action on Smoking and Health (ASH) Margaret Pyke House, 27-35 Mortimer Street, London, W1A 4QW; and The Chest and Heart Association, Tavistock House North, Tavistock Square, London, WC1.

6. BLOOD PRESSURE

6.1

In the United Kingdom, as in most populations, blood pressure levels rise with increasing age and elevated blood pressure is common in adults. The definition of what constitutes hypertension is arbitrary. Large screening surveys among middle-aged men in London have found the prevalence of casual diastolic pressures of 90 mm Hg or above to be around 40 percent, while pressures of 115 mm or above have been found in about 3 percent (2 percent at 40 to 49 years, 4 percent at 50 to 59 years and 6 percent at 60 to 64 years). More than half of these cases were previously unrecognised and only one-fifth were already under care for hypertension. A community study in Scotland revealed that 16 percent of subjects aged 45 to 64 years had a casual diastolic blood pressure over 100 mm Hg and one-third of these had pressures still in this range on early follow-up. As in London, 40 percent of the population had initial diastolic pressure of 90 mm Hg or more. Studies in general practice have shown similarly high rates. In one general practice in an industrial Welsh village 98 percent of persons aged 20 to 64 were screened and 6 percent of both men and women aged 40 years or more were found to have sustained diastolic pressures exceeding 105 mm in men and 115 mm Hg in women.

A large prospective survey in South Wales has emphasised the prognostic importance of even moderately elevated diastolic blood pressure.

Table 3. Incidence rates (per 1000 person-years) of all cardiovascular deaths, non-fatal strokes and myocardial infarction in subjects aged 35 to 64 years according to diastolic blood pressure (mm Hg)

	< 90	90-109	110 and over
Men	7.7	19.3	68.5
Women	4.7	11.4	35.7

The figures quoted in Table 3 referred to diastolic pressures measured at the point of muffling (phase 4). Use of the point of disappearance of sounds (phase 5) yields measurements that on average are about 4 mm lower, corresponding to prevalence rates approximately half those quoted. The relative merits of the two end-points have long been in dispute and medical practice in this and other countries is divided. In addition, there are large systematic differences in blood

pressure according to the circumstances in which it is measured; levels tend to be higher in hospital and population surveys than when measured in general practice or at home. Similarly, the values tend to fall substantially over a series of follow-up visits. Guide lines for investigation and treatment must take these various factors into account.

6.2 Role as a risk factor

Prospective epidemiological studies have consistently shown that a single blood pressure reading is a powerful indicator of the risk of CHD. As a risk factor the first reading of systolic pressure seems to be at least as predictive as either diastolic pressure or the mean of readings made at several different examinations.

Figure 11, derived from the 16-year follow-up results of the Framingham Study, illustrates how well CHD risk can be identified even by a systolic reading made under so-called "casual" conditions at the initial examination. The risk increases continuously over the whole observable range of blood pressure with no evident threshold. For men in their forties, CHD incidence increases by nearly 20 percent for each 10 mm increase in systolic pressure, so that at 160 mm the risk is almost twice that at 110 mm. At levels exceeding 180 mm the risk gradient becomes even steeper. As age advances, hypertension becomes more prevalent and its dire significance does not diminish. For women, it carries a roughly similar relative risk, but its danger in absolute terms is diminished by the generally lower incidence of CHD.

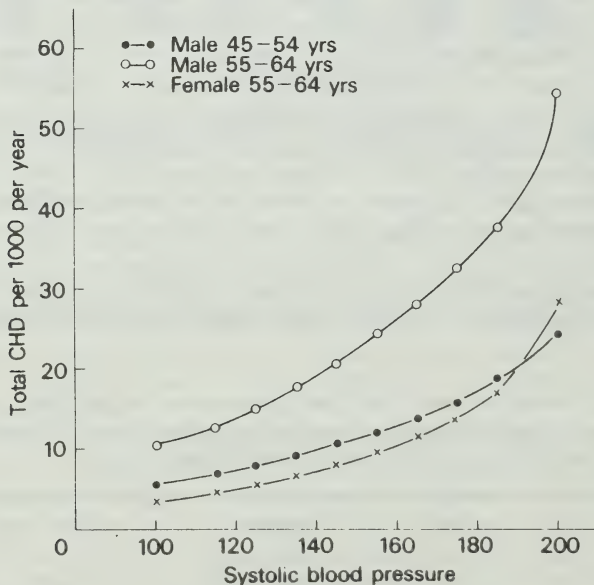


FIGURE 11.—CHD incidence (average over a 16-year period) in relation to blood pressure at initial examination (Kannel and Gordon, 1970).

The individual patient with severe hypertension (as seen commonly in clinical practice) faces a specially high risk, mainly of stroke and left ventricular failure. However, such cases contribute only a small proportion to the total burden of CHD in the community; it is mild undiagnosed hypertension that, because it is so much more prevalent, contributes most to the occurrence of CHD. Figure 12 illustrates this

point and shows the contribution of hypertension-associated risk to the total incident of CHD in a community. From the community point of view the greater part of this effect relates to very mild hypertension (diastolic pressure < 100 mm).

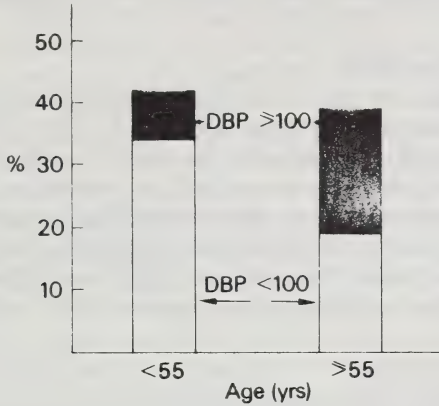


FIGURE 12.—Percentage of total CHD in males associated with hypertension. Data on CHD risk from Framingham Study (Kannel and Gordon, 1970) and on the distribution of blood pressure in the population from Hamilton et al., 1954.

6.3 Relation to other risk factors

The effect of blood pressure on the risk of CHD is much greater (in absolute terms) in the presence of smoking or raised level of plasma cholesterol (see Fig. 7), and probably also in persons who are physically inactive. Thus, if risk is doubled for a man who smokes cigarettes and doubled also for a man with systolic pressure of 160 mm, then it is almost quadrupled for a man with both of these risk factors; the separate relative risks must be multiplied. Risk is further increased if there is ECG evidence of left ventricular hypertrophy. This means that the risk associated with hypertension depends very much on the levels of these other risk factors. This is illustrated in Fig. 13, where, for men aged 45, it can be seen that the excess incidence associated with a systolic pressure of 180 mm will involve, over a 10-year period, about 6 out of every 100 non-smokers, but about 9 out of every 100 cigarette smokers.

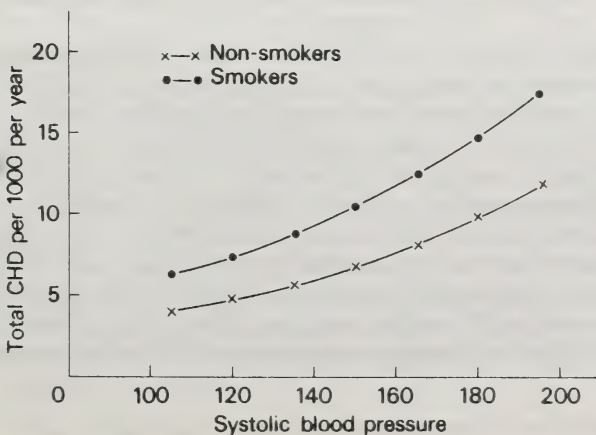


FIGURE 13.—The CHD risk in hypertension and its relation to smoking (Gordon et al., 1971).

In view of the strength and consistency of the association between CHD and blood pressure, and its relative independence of other risk factors, it is clearly a critically important contributor to the development of CHD. It appears to operate largely by accelerating atherogenesis but ventricular hypertrophy may aggravate myocardial ischaemia.

6.4 *Reversal of the factor*

Raised blood pressure can be controlled with varying degrees of success by the established measures, notably by drugs that lower blood pressure. These should not usually be started until an adequate baseline has been established by repeated measurements. In more severe hypertension it is necessary to use drugs that commonly produce adverse effects; adherence to treatment is often poor, and sustained reduction of blood pressure is unusual. Milder hypertension requires less potent drugs and adherence can be good even among symptomless subjects.

6.5 *Reversibility of risk*

Randomised controlled trials among middle-aged men have shown a large overall benefit from treatment due chiefly to a reduced incidence of stroke and left ventricular failure. This benefit has been so large that trials have been terminated on ethical grounds at a stage when there were few cases by which to assess the effect on CHD risk. The U.S. Veterans Administration trials studied men with sustained diastolic hypertension of 90 mm and above. At the time of termination of the studies the position was as shown in Table 4.

Table 4.

	Number of Patients	
	Treatment	Control
Patients in trial	259	264
Total hypertensive complications	24	83
Fatal MI/sudden death	6	12
Non-fatal MI	5 } 11	4 } 16

At this stage there were only half as many CHD deaths in the treatment as in the control group but this difference is within chance limits. Thus, at the present time there is no clear evidence that treatment of hypertension will reduce the risk of CHD. This important issue will only be settled by much larger controlled trials in patients with less severe hypertension among whom a higher proportion of complications is attributable to CHD. Such trials are now in progress but results will not be known for several years. Trials are also in progress to test whether the metabolic and neurological effects of certain anti-hypertensive drugs (thiazides and beta-blockers) influence the risk of CHD, apart from the direct consequences of their hypertensive actions.

6.6 Conclusions and recommendations

1. The finding of even mild hypertension identifies an individual as being at much increased risk of CHD. He is also more susceptible to the effects of other risk factors and the benefits from correcting other risk factors can be expected to be correspondingly greater than in normotensive persons. This means that regardless of whether or not hypertensive drugs are prescribed, the control of smoking, diet and physical inactivity takes on a special importance in every person in whom the blood pressure is above normal.

2. The detection and treatment of symptomless hypertension is fully justified on grounds of reducing the risk of stroke and other complications. We are unlikely to know for some time what additional effect there may be on the risk of CHD. Hospital doctors and general practitioners alike have considerable opportunities for blood pressure screening that at present are under-exploited. It is recommended that subjects should rest for five minutes before the initial measurement. If this is raised (diastolic over 90 mm²) it should be repeated. If the mean of these two readings reaches the treatment level, the pressure measurement should nevertheless be repeated on one or, preferably, two subsequent occasions before long-term hypotensive therapy is begun.

3. A high reading of blood pressure at the patient's initial visit constitutes evidence of high CHD risk, justifying surveillance and attention to other risk factors, but it is an insufficient basis for giving hypotensive drugs. Such treatment has been shown to be of value only in persons with sustained hypertension. If the pressure approaches the recommended treatment level it should be checked annually.

4. Pending the outcome of further trials it may be reasonable to take as a general therapeutic guide line a diastolic pressure in men under the age of 65 averaging 100 mm Hg* or above. Adjustments to this criterion may be appropriate in order to take account of associated risk factors and other individual characteristics. In women under the age of 65 the level for treatment may be taken as 5 to 10 mm higher, and over the age of 65 in either sex it may be 10 to 20 mm higher. Those with pressures approaching but not reaching the treatment level should be reviewed annually. At the present time, treatment is not recommended in individuals with isolated systolic hypertension, since we have insufficient knowledge of either the risks or the benefits of treatment.

7. OBESITY

7.1 Introduction

There is a widespread public belief that obesity is an extremely important risk factor in the causation of CHD. Since 1968 at least 12 official bodies have made recommendations on dietary and other measures to reduce the risk of CHD and all have advised some measures to prevent and/or treat obesity by diet and/or exercise. Yet the original epidemiological data on which all the recommendations are based show that the risk of CHD associated with obesity is modest compared with other factors such as elevated plasma cholesterol level, raised blood pressure and cigarette smoking. In this section we discuss the apparent contradiction and try to explain why obesity is considered to be important in CHD.

* Phase 5. Those using phase 4 should add approximately 4 mm to these criteria.

The desirable weight in an individual is presumably that associated with the lowest mortality rate. There are no desirable weight tables available for the United Kingdom population and the tables most commonly used are those derived from the U.S.A., which take into account sex and height and body frame (Table 5). The results may be expressed as a percentage of the desirable weight, and persons who are 20 percent or more overweight compared with their desirable weight are considered to be excessively heavy or obese.

Table 5. Desirable weight of adults according to height and frame. Based on weights of insured persons in the U.S.A. associated with lowest mortality (Macleod, 1974).

Height without shoes			Desirable weight in kilograms and pounds (in indoor clothing), ages 25 and over					
			Small frame		Medium frame		Large frame	
metres	ft	in	kg	lb	kg	lb	kg	lb
Men								
1.550	5	1	50.8-54.4	112-120	53.5-58.5	118-129	57.2-64	126-141
1.575	5	2	52.5-55.8	115-123	54.9-60.3	121-133	58.5-65.3	129-144
1.600	5	3	53.5-57.2	118-126	56.2-56.7	124-136	59.9-67.1	132-148
1.625	5	4	54.9-58.5	121-129	57.6-63	127-139	61.2-68.9	135-152
1.650	5	5	56.2-60.3	124-133	59 -64.9	130-143	62.6-70.8	138-156
1.675	5	6	58.1-62.1	128-137	60.8-66.7	134-147	64.4-73	142-161
1.700	5	7	59.9-64	132-141	62.6-68.9	138-152	66.7-75.3	147-166
1.725	5	8	61.7-65.8	136-145	64.4-70.8	142-156	68.5-77.1	151-170
1.750	5	9	63.5-68	140-150	66.2-72.6	146-160	70.3-78.9	155-174
1.775	5	10	65.3-69.9	144-154	68 -74.8	150-165	72.1-81.2	159-179
1.800	5	11	67.1-71.7	148-158	69.9-77.1	154-170	74.4-83.5	164-184
1.825	6	0	68.9-73.5	152-162	71.7-79.4	158-175	76.2-85.7	168-189
1.850	6	1	70.8-75.7	156-167	73.5-81.6	162-180	78.5-88	173-194
1.875	6	2	72.6-77.6	160-171	75.7-83.9	167-185	80.7-90.3	178-199
1.900	6	3	74.4-79.4	164-175	78.0-86.2	172-190	82.6-92.5	182-204
Women								
1.425	4	8	41.7-44.5	92-98	43.5-48.5	96-107	47.2-54	104-119
1.450	4	9	42.6-45.8	94-101	44.5-49.9	98-110	48.1-55.3	106-122
1.475	4	10	43.5-47.2	96-104	45.8-51.3	101-113	49.4-56.7	109-125
1.500	4	11	44.9-48.5	99-107	47.2-52.6	104-116	50.8-58.1	112-128
1.525	5	0	46.3-49.9	102-110	48.5-54	107-119	52.5-59.4	115-131
1.550	5	1	47.6-51.3	105-113	49.9-55.3	110-122	53.5-60.8	118-134
1.575	5	2	49 -52.6	108-116	51.3-57.2	113-126	54.9-62.6	121-138
1.600	5	3	50.3-54	111-119	52.6-59	116-130	56.7-64.4	125-142
1.625	5	4	51.7-55.8	114-123	54.4-61.2	120-135	58.5-66.2	129-146
1.650	5	5	53.5-57.6	118-127	56.2-63	124-139	60.3-68	133-150
1.675	5	6	55.3-59.4	122-131	58.1-64.9	128-143	62.1-69.9	137-154
1.700	5	7	57.2-61.2	126-135	59.9-66.7	132-147	64 -71.7	141-158
1.725	5	8	59 -63.5	130-140	61.7-68.5	136-151	65.8-73.9	145-163
1.750	5	9	60.8-65.3	134-144	63.5-70.3	140-155	67.6-76.2	149-168
1.775	5	10	62.6-67.1	138-148	65.3-72.1	144-159	69.4-78.5	153-173

7.2 *Risk of coronary heart disease*

From the life insurance experience of several million North Americans insured between 1935 and 1953 an excess mortality from CHD of 35 percent for men who were 20 percent or more above average weight has been observed. Community-based studies in America (Framingham) have also shown an increased risk of CHD with increasing obesity, although in this particular community study the effect of obesity on CHD risk was less than the effect of raised plasma cholesterol level or high blood pressure. In London busmen, obesity was also associated with an increased CHD incidence but this was far less than that associated with raised levels of plasma cholesterol or blood pressure.

A relationship between obesity and CHD has not been observed in all studies, and in some, excess weight has carried an increased risk in men but not in women. The relationship has also been noted to be more evident with angina and sudden death than with non-fatal myocardial infarction. In comparing different national groups obesity does not help to explain the difference in CHD incidence between the populations. The relationship between obesity and CHD is clearly not consistent and appears to be less important than raised plasma cholesterol levels or high blood pressure.

7.3 *Relationship with other risk factors*

Obesity is usually associated with the presence of other risk factors for CHD, including increased blood pressure, glucose intolerance or diabetes mellitus, physical inactivity and raised plasma levels of triglycerides, cholesterol and uric acid. When these associated risk factors are held constant the predictive value of obesity on its own is much reduced in relation to CHD. This seems to indicate that if obesity increases CHD then it operates largely through these associated factors. This does not imply that obesity should be disregarded. It is more readily recognised than high blood pressure, raised plasma lipid levels of glucose intolerance and the medical practitioner confronted with an obese individual in our society can assume that there is at least a moderately increased risk of CHD.

7.4 *Reversibility of obesity*

In theory, obesity is easy to treat by eating less and by exercising more. In practice, most obese patients do not readily or seriously try to reduce weight and those who do lose weight will usually regain it. It is for this reason that all health authorities emphasise the importance of preventing obesity or treating it enthusiastically in the early stages. In the last ten years there appears to have been a modest improvement in the prospects for weight reduction partly because of the involvement of enthusiastic lay groups. Good results can be obtained in general practice, and in one five-year study about one-third of patients lost weight and maintained their weight loss, one-third lost weight but regained it, and one-third did not lose weight at any time. These results show what can be achieved as a consequence of special interest, but they are still not satisfactory.

7.5 *Reversal of CHD risk on weight reduction*

There is no reliable evidence that weight reduction is followed by a reduced incidence of CHD and it remains an assumption that weight

reduction by itself will have an effect on the incidence of CHD. Correction of obesity is desirable because of its close association with hypertension, hyperlipidaemia and glucose intolerance, and for many other reasons not directly associated with CHD, such as mechanical disability, accidents, respiratory and skin disorders, emotional problems and a general increase in mortality.

7.6 *Conclusions*

1. Obesity is associated with an increased mortality in general and may be associated with an increased risk of some forms of CHD.

2. Obesity is commonly associated with hypertension and glucose intolerance (diabetes mellitus) and in the presence of these factors and/or of raised plasma cholesterol levels, obesity becomes a risk factor for CHD. Where obesity is completely unassociated with any other risk factors (which is probably unusual) it is apparently not an important risk factor for CHD.

3. Correction of obesity will beneficially affect glucose intolerance, blood pressure and plasma lipid levels, particularly of triglycerides. For these reasons alone it is desirable, despite the lack of direct evidence that weight reduction by itself will lower the risk of CHD.

7.7 *Recommendations*

1. Obese people should be screened for the presence of other more potent risk factors, e.g. hypertension, hyperlipidaemia and diabetes mellitus, and details of cigarette smoking and family history should be ascertained.

2. The emphasis to be placed on weight reduction in the obese individual will depend to a considerable extent on the presence or absence of other risk factors for CHD. There is a limit to the number of modifications an individual is likely to make at the same time in his life style, and, in some individuals, modification of other factors should take precedence over weight reduction. Thus, cigarette smoking, hypertension and high blood cholesterol levels require more specific and immediate attention than obesity.

3. In clinical practice the aim should be to see that as far as possible the patient does not exceed the desirable weight (Table 5).

4. *Weight reducing diets.*—Two types are in general use: those very low in carbohydrates and those that prescribe a reduction of all the components of the diet.

(a) Very low carbohydrate diets usually contain an increased proportion of fat, and advocates of these diets often maintain that fats can be eaten freely as long as carbohydrate intake is restricted. However, such diets produce an increase in plasma cholesterol level and are not recommended.

(b) A diet in which all the components are reduced is recommended. Particular attention is drawn to a reduction in the intake of sugar and alcohol as these are very common sources of excess energy intake. A combination of exercise and diet is strongly recommended and, where necessary, the help of a dietitian should be invoked.

5. *Physical Activity.*—A certain minimum amount of exercise is necessary for satisfactory weight reduction. Regular daily exercise is much more valuable in weight reduction than spurts of activity at the

weekend. In many very obese subjects, only mild forms of physical exercise are possible and if there is no medical contra-indication, most overweight subjects can benefit from walking. Walking for an hour a day at a modest pace (3 mph) could result in the expenditure of 300 kcal (1.3 MJ). The benefits of exercise should not distract attention from the need to reduce food intake.

8. PHYSICAL ACTIVITY

8.1 *Introduction*

There is widespread acceptance that man derives benefit from habitual physical activity (exercise) but there is no clear evidence regarding just how much physical activity—in terms of intensity, duration, frequency or type of exercise—is required to produce a measurable benefit to health. In recent years there has been considerable interest in the role of sedentary living on the development of CHD and evidence suggesting that physical activity may be a significant factor in cardiovascular health is accumulating.

8.2 *Role as a risk factor*

1. *Work Activity.*—Evidence from many countries indicates that men in physically active occupations derive some protection against CHD but other studies have failed to confirm this finding. In eastern Finland, for example, a country with the highest CHD mortality rate in the world, it is clear that heavy work is not protective when other risk factors for CHD are prominent. Studies of London busmen by Morris and his colleagues 20 years ago produced the first evidence for the protective effect of exercise on the heart, with active bus conductors experiencing fewer CHD events than sedentary bus drivers. Similarly, postmen were found to suffer far fewer heart attacks than clerks and other sedentary Post Office workers. However, it was not clear to what extent the differences in CHD experience were due to their different jobs or due to the fact that the men were different kinds of individuals. In the final analysis, when allowances were made for differences in physique, blood pressure and plasma cholesterol, there still remained a substantial difference in CHD incidence between the physically active and inactive workers. The most recent report of work activity and CHD mortality concerns U.S.A. dock workers who were classified as being in high, medium or low caloric-output jobs and followed for 22 years (or to death or age 75 years). Annual reclassification allowed for the effect of changing type of work (Fig. 14). The high activity workers had CHD death rates almost half those found in medium and low categories: there was little difference between medium and low category workers. This association was seen especially for sudden death (which was about three times as frequent in the moderate and light worker categories), an observation previously made in the busmen and postmen. The difference in CHD mortality between heavy and light work groups persisted when the effects of other risk factors (smoking, blood pressure, obesity, previous heart disease, glucose intolerance) were taken into account. It has been suggested from this study and several others that repeated bursts of high energy output establish a plateau of protection against coronary mortality. However, such activities are now increasingly uncommon and other studies have shown the apparent value of lesser grades of activity.

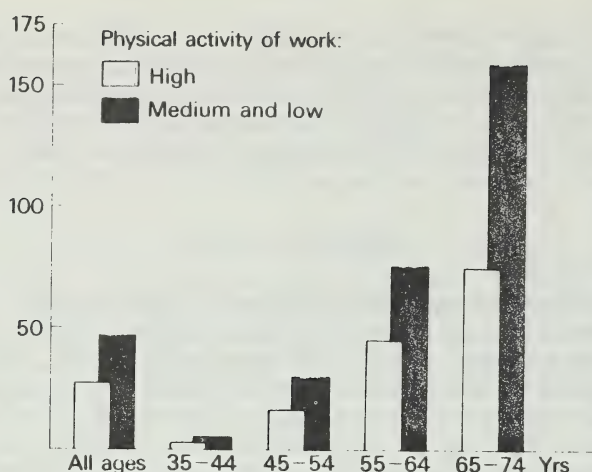


FIGURE 14.—Coronary heart disease death rates/10,000 man-years of work according to physical activity at work and age at death (Paffenberger and Hale, 1975).

2. *Leisure Activity*.—Few people are nowadays engaged in vigorous occupational activity, and work in advanced societies increasingly is light and sedentary. Leisure time activity may become the major source of exercise and thus any contribution to public health can only come from leisure time activity. In a recent social survey it was found that after leaving school and by the age of 22 years, only 27 percent of men cited regular physical recreation as the chief leisure activity, 20 percent after marriage, and 10 percent after the first child was born. For women, the figures were 28 percent, 10 percent, and 2 percent respectively. There may also be considerable social class difference in the amount of active recreation taken by adult men. A study in southern England showed that semi-skilled and unskilled workers took the least active recreation (swimming, football, tennis, squash, athletics), skilled workers were intermediate and the professional men took the most exercise.

A recent study of middle-aged sedentary male civil servants has shown a striking difference in the relative risk of CHD between men reporting different levels of leisure activity. Men recording vigorous exercise had about one-third the incidence of CHD experienced by comparable men who did not. The suggestion from this study is that vigorous activities protect against CHD events in middle age. Vigorous exercise includes swimming, "keep-fit" exercises, jogging/running, brisk walking, cycling, climbing many stairs and really heavy work in the garden, house or garage (Fig. 15).

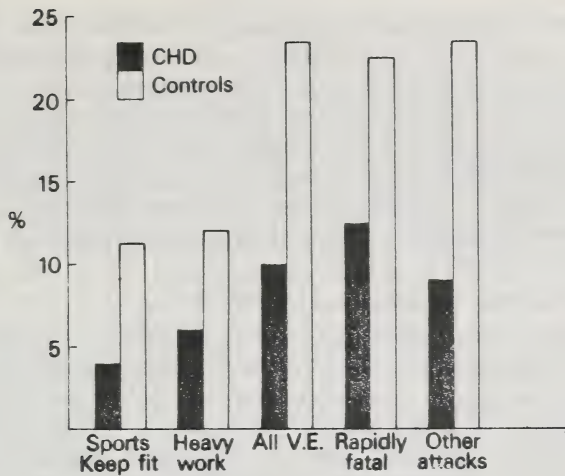


FIGURE 15.—Percentage of men reporting vigorous exercise in leisure time. Executive grade civil servants 40 to 65 years with first clinical attacks of CHD and matched controls (Morris *et al.*, 1973).

3. *Mechanisms.*—Although many studies have demonstrated an association between exercise and CHD there is no proof that the association is causal. However, theoretical considerations could explain a protective effect of physical activity. Regular exercise, especially if vigorous, improves cardiopulmonary function and exercise tolerance. Heart rate and blood pressure responses to exercise are reduced by training and, as a result, so is ventricular work. Myocardial anastomotic and collateral arterioles are increased in size. In addition, vigorous activity increases fibrinolytic activity and affects platelet behaviour, and there are claims for its beneficial effects on hypertension, hyperlipidaemia, tachycardia and obesity.

8.3 Relationship to other risk factors

There is little relationship between the reported taking of regular vigorous exercise and the levels of plasma cholesterol but an increase in physical activity has a favourable effect of plasma triglycerides and can reduce both fasting levels and the increased levels accompanying postprandial lipaemia. Provided calorie intake remains unchanged, weight loss is encouraged by exercise.

There has been no adequate study of the effect of long-term training on blood pressure or hypertension, and data on cerebrovascular disease relative to physical activity are inconclusive. Those who value physical fitness are unlikely to be heavy smokers and exercise increases the elimination of carbon monoxide. The situation in eastern Finland strongly suggests that in the presence of very high levels of other risk factors such as plasma cholesterol, blood pressure and cigarette smoking, even considerable physical exercise is not protective against the risk of CHD.

8.4 Reversal of physical inactivity

Physical inactivity is potentially reversible but, as occupations are becoming increasingly sedentary, an increase in physical activity will

usually require a major change in the use of leisure time. Such changes in behaviour are unlikely in the absence of strong motivation or where there are few opportunities to exercise in pleasant and convenient circumstances. Many programmes designed to encourage physical fitness in healthy middle-aged men have had a high drop-out rate, especially when they involve attendance at a special centre. The problems of motivation and choice of exercise have not been solved and will require health education together with personal persuasion by the medical and allied professions.

8.5 *Exercise in the prevention of CHD*

A full-scale randomised controlled trial of exercise in the prevention of CHD is a theoretical but not a practical possibility because of its complexities and cost, and advice in this field must be based on the available evidence. The rewards of increased physical activity include improved exercise tolerance and an enhanced physical and mental well-being, and the evidence suggests that it is likely to benefit health.

8.6 *Recommendations*

1. There is sufficient evidence to justify a major concern about the sedentary life in relation to CHD and to justify efforts to encourage the habit of physical activity at all ages and in both men and women. This seems reasonable and prudent even though we have no definitive evidence regarding just how much physical activity or what degree of physical fitness is required to protect against CHD.

2. All forms of rhythmical dynamic exercise, especially those using larger muscle groups, are beneficial if energetic. They include brisk walking, climbing stairs or hills, running, jogging, swimming, cycling and playing games such as tennis, badminton or squash. Most of these activities can be carried out throughout the year and at all ages. Simple exercises (callisthenics) are valuable in improving joint mobility and muscle strength and are an important preliminary for those wishing to take more vigorous exercise. Isometric exercises such as weight-lifting or press-ups are of little value for improving cardiopulmonary fitness as they cannot be sustained and invoke little oxygen consumption. Such exercises, and isometric exertion such as carrying heavy loads or moving heavy furniture, may on occasions be dangerous because of the associated steep rise in blood pressure.

3. *Medical examination.*—Most people do not need a medical examination before starting an exercise programme. There are no risks in regular dynamic exercise as long as the programme begins gently and only gradually increases in vigour. Older persons, the obese and those with a history of cardiovascular disease or symptoms should first consult their doctor. Those who develop unexpected symptoms during exercise should also seek medical advice.

4. After a myocardial infarction, it is good medical practice to encourage the patient to return to work and to his former recreational activities wherever this is not specifically contra-indicated. A programme of graded exercise should be encouraged both for its physical and psychological benefits. However, light, regular unsupervised exercise is probably better than none at all and may well be the most acceptable and beneficial to the majority of CHD subjects.

Some suggestions for exercise are provided in Appendix 3.

9. STRESS

9.1 Introduction

1. This section is concerned with emotional and psychological factors in relation to coronary heart disease and involves discussion of personality and of social and behavioural characteristics. Most physicians and lay people believe that the behavioural and emotional aspects of life are related to the development of heart attacks and include stress among the important risk factors for CHD.

2. The term stress in this context relates to the individual's response to nervous tension and to the emotions aroused by occupational and domestic anxieties. These anxieties are commonly associated with environmental situations inducing frustration, fear, hostility and insecurity.

3. The belief that stress is a risk factor for CHD is largely based on clinical experience and most of the extensive literature concerns studies of persons already affected by clinical CHD. Only one study (in the U.S.A.) shows an independent association of behaviour type with future CHD risk and no such studies have been reported in the United Kingdom, or indeed outside the U.S.A. Despite our beliefs and impressions, it has not yet been demonstrated that there is a readily measurable (or modifiable) behavioural factor in CHD risk.

*9.2 Stress as a risk factor for CHD**9.2.1 Behaviour patterns*

An increased frequency of CHD has been reported among American men and women with certain patterns of behaviour. Type A behaviour, characterised by excessive sense of time urgency, preoccupation with deadlines, aggressiveness and competitive drive, is regarded as a risk factor for CHD in contrast to Type B which has the opposite characteristics. Similar descriptions have been presented from Australia, the Netherlands and Sweden, but not from the United Kingdom. From a prospective study in the U.S.A. it is claimed that Type A men have twice the risk of CHD after account has been taken of the other well-recognised risk factors. The claims by the originators of the Type A hypothesis tend to be overstated and there is no general agreement at present that a particular type of personality or behaviour is a necessary component of CHD, even in Western culture. This is not to deny that individual or group behaviour may be related to pathogenesis or to the precipitation of acute events in susceptible subjects. The hypothesis linking types of behaviour and personality to CHD is unlikely to be tested experimentally and, since behaviour and personality cannot at present be satisfactorily measured or effectively modified, this hypothesis does not help in the prevention of CHD in the community. Appreciation of the type of personality that may be at higher risk from CHD may, however, be of use in the counselling of particular individuals considered to be at high risk of CHD because of the presence of other well established risk factors.

9.2.2 Environmental and social change

Several studies in the United States have indicated that the CHD risk increases with major changes in place of residence or in occupation and where there are marked discrepancies between the individual's social background and his present social status. The risk of

CHD appears to increase among people who move into unfamiliar social circumstances. The risk may increase because of the type of person who moves around, because of the change itself, or because of the situation to which the person moves. Where subjects do not change their residence or occupation but where social or environmental changes occur in the situation in which they work or live, CHD mortality may also increase. All these associations are indirect and it is uncertain whether we are observing the effect of mobility or the selective bias of those who move.

9.2.3 Life events

Some studies have related CHD to preceding stressful life events such as bereavement, accidental injury, loss of employment, serious illness, premature retirement or major disappointments. Almost all the studies have been retrospective, i.e. concerned with people with recognised CHD, and many different life events have been associated with the various manifestations of CHD. Prospective studies on life events and illnesses that have been reported are difficult to evaluate. Death of a spouse and loss of employment seem to be particularly important factors.

9.2.4

It is well recognised that acute emotion may occasionally precipitate angina pectoris, myocardial infarction, arrhythmias and sudden death in susceptible individuals.

9.3 Relation to other risk factors

There are many possible ways in which social and psychological factors may be implicated in the development or manifestation of CHD. The neuro-endocrine system has been shown to affect catecholamine and cortisol excretion, blood pressure, heart rate, lipid metabolism, salt regulation and myocardial metabolism. Catecholamines mobilise stored triglyceride as free fatty acids. Excess free fatty acids can increase the oxygen debt of a potentially ischaemic myocardium and lead to arrhythmias and impaired contractility. Excess free fatty acids, unused as fuel, can also lead to increased plasma triglycerides and cholesterol esters and these may be laid down in the arterial wall.

While there is little doubt that stress may be accompanied by some or all of these changes, there is at present no firm evidence that they lead to arterial wall changes or to CHD.

9.4 Reversal of stress

1. It may be possible to alter certain easily recognised situations arising from occupational or domestic circumstances. There is no evidence that such a reversal of a stressful situation will necessarily reduce the risk of CHD. Nevertheless, the management of stress is a part of good medical practice and the doctor should be able to recognise certain patterns of behaviour from discussions with the patient and with his family.

2. Where the outward signs of stress are found in the individual or in the family as a whole it may be possible to improve the situation by counselling. Explanation of the relationship between stress and CHD may be of value, particularly where other risk factors are present.

9.5 *Conclusions/recommendations*

1. While acute stress may occasionally precipitate a heart attack in susceptible individuals, it is difficult to prove that chronic stress contributes to the development of CHD.

2. Although it cannot be established that advice given to individuals about stress will reduce their risk of CHD, there is enough evidence to indicate that physicians should counsel their patients about the stress in their lives, especially when other risk factors such as high blood pressure and smoking are present at the same time. These stresses may be domestic or occupational or may predominantly reflect the individual's personality. Counselling of these individuals regarding stress may be of value to them and the success of such counselling will depend to a considerable extent on the individual doctor and on the particular patient.

3. Initiative, diligence, leadership and hard work, especially in young people, should not be discouraged on the mistaken supposition that these qualities are indicative of future CHD.

10. DIABETES AND CORONARY HEART DISEASE

10.1 *Diabetes and arterial disease*

In Western cultures diabetic men have 2 to 3 times more CHD and diabetic women 5 to 6 times more than corresponding non-diabetics. Among Western diabetics CHD is the single commonest cause of death, accounting for about 50 percent of them. Increased frequency of atherosclerotic disease occurs in both major clinical varieties of diabetes, the insulin-dependent (juvenile type) and non-insulin dependent (maturity-onset type). In the former, microvascular disease also contributes to morbidity and mortality. In the latter, coronary heart disease, cerebrovascular disease (CVD) and peripheral vascular disease (PVD) are preeminent.

When large population samples in Western countries are subjected to glucose tolerance testing, the spectrum of response ranges from the majority who are clearly normal to the 2 to 3 percent of the population with clear diabetic responses. Approximately 10 percent have intermediate responses, or borderline diabetes. Susceptibility to arterial disease appears to rise in parallel with increasing glucose intolerance. This may partly be due to association with other risk factors for CHD.

In certain geographically defined ethnic groups, e.g. Japanese and Africans, in which atherosclerosis and its complications are generally uncommon, there appears to be a very low susceptibility to CHD in diabetic subjects, but diabetes still appears to increase the risk of arterial disease.

10.2 *Diabetes as an independent risk factor*

Diabetes, including borderline varieties, is associated with obesity, elevation of plasma lipids, hyperinsulinaemia and, possibly, hypertension. The treatment of diabetes often includes the recommendation of a low carbohydrate, high-fat diet that may well be atherogenic. Oral anti-diabetic agents have been reported to increase the risk of cardiovascular death, and even insulin has been accused of increasing the risk of arterial disease. Increased CHD in diabetes may thus be—

- (a) An effect of the diabetic state;
- (b) a consequence of anti-diabetic therapy;
- (c) due to recognised risk factors occurring with increased frequency in diabetes or the potentiation of these risk factors by the associated diabetes.

10.2.1 *The importance of diabetes*

In view of the considerable variation in CHD prevalence in diabetics in various ethnic or geographic groups, the diabetic state by itself cannot be regarded as a critical factor for CHD. Those risk factors known to be strongly associated with the varying incidence of CHD in non-diabetics in various cultures probably account for the parallel variation in the diabetic.

10.2.2 *The consequences of anti-diabetic therapy*

There is no clear evidence that the degree of metabolic control of diabetes, as measured by blood sugar concentrations, influences the risk of developing atherosclerosis. The dietary regime recommended for the Western diabetic commonly employs reduction of carbohydrate and replacement with fats, often of dairy origin. National groups of diabetics (e.g. Japanese) who, for economic and cultural reasons, take proportionately higher carbohydrate diets are less prone to CHD but inferences must clearly be guarded.

The oral anti-diabetic agents, tolbutamide and phenformin, have lately been the subject of controversy in relation to cardiovascular mortality in diabetics. In America, a major controlled trial with random allocation to various treatments has claimed a significant excess of death from cardiovascular causes in asymptomatic, maturity-onset diabetics treated with oral agents. Other smaller studies employing random allocation either fail to confirm this finding or challenge it.

10.2.3 *Recognised risk factors for CHD in the diabetic*

(a) *Obesity*.—The general uncertainty regarding the importance of obesity as a risk factor in CHD also applies to the diabetic subject. In the American study, relative weight at the start of the study was not related to cardiovascular mortality. In an English study (Bedford), the follow-up of borderline diabetics showed that relative weight influenced the frequency of angina but did not affect ECG changes. However, as in non-diabetics, the reduction of obesity may also bring about reduction in associated risk factors.

(b) *Hyperlipidaemia*.—There is much evidence of the increased frequency of hyperlipidaemia in the clinical diabetic, often associated with obesity and usually manifest by raised triglyceride levels and, occasionally, with hypercholesterolaemia. Elevation of both these plasma lipids in non-diabetics is associated with increased future risk of CHD, but there has been little examination of such a predictive role in diabetics. Nor is it known whether a given degree of hyperlipidaemia constitutes a greater risk to the diabetic than to the non-diabetic. However, diabetics with arterial disease have higher serum lipids than those without.

(c) *Hypertension*.—Although no systematic tendency to hypertension has been found in several adequately controlled studies of diabetics, a study of an American industrial population revealed raised arterial pressure more often in diabetics than in non-diabetic controls

even before the diagnosis of the diabetes, allowing for age, sex and body weight.

In summary, diabetes is associated with an increased risk of CHD. Much of this is probably due to the greater frequency in the diabetic population of other known risk factors for CHD. In addition, the diabetic state appears in some way to aggravate the effect of these risk factors and their reversal may thus achieve a more striking reduction of atherosclerotic disease in diabetics (particularly women) than in non-diabetics.

10.3 Is the risk factor reversible?

There is, unfortunately, no evidence that present methods of anti-diabetic treatment reduce the enhanced risk of CHD in the diabetic. Complete normalisation of blood sugar and associated metabolic disturbances is, however, rarely achieved. If treatment of diabetes were widened to include active measures to reduce or reverse the risk factors discussed above, the rate of CHD might be considerably lessened.

10.4 Recommendations

1. Reversal of known risk factors should be pursued energetically in diabetic subjects. Blood pressure, plasma lipids and body weight should be periodically re-assessed and controlled, perhaps even more strictly than in the non-diabetic. Cigarette smoking should be strongly discouraged.

2. Dietary policy should be specific to the individual and determined as much by the plasma lipids as by the blood sugar levels. Disproportionate carbohydrate restriction may increase fat intake and lead in some patients to increased plasma lipids. Some authorities recommend provision of at least 50 percent of food energy as carbohydrate. Reduction of plasma lipids should be sought by dietary change or where necessary by drugs. Partial substitution of saturated fats by polyunsaturated fats and vegetable oils is recommended in the diabetic diet.

3. Although people with lesser degrees of glucose tolerance have an increased risk of CHD, this does not justify widespread screening for blood sugar levels. Conventional urine testing for glycosuria will rarely fail to disclose clinically significant diabetes.

11. ORAL CONTRACEPTIVES

11.1

Some recent figures suggest that CHD is increasing in frequency in women under the age of 45 years. The majority of such women have at least one of the risk factors associated with the premature occurrence of the disease in men, such as hyperlipidaemia, hypertension or cigarette smoking. It is probable that oral contraceptives add significantly to the risk of developing CHD only in those who are already at increased risk. It constitutes a negligible risk in women under the age of 40 who are without risk factors for CHD.

11.2

Recent reports indicate that the risk of developing non-fatal myocardial infarction or coronary death is between 5 and 6 times as high in women aged 40 to 44 years who use oral contraceptives compared with non-users. The actual annual risk of death is in the region of

60/100,000 compared with 10/100,000. There was more myocardial infarction in women currently using an oral contraceptive than in those who were ex-users or who had never used a contraceptive pill.

11.3

Oral contraceptives can lead to hypertension but in the majority this is reversible after withdrawal of the drug. Women who become hypertensive are mostly those with labile hypertension and many have had hypertension or even pre-eclampsia during a previous pregnancy.

11.4

Carotid and cerebrovascular thromboses have occurred sufficiently often in women who are not hypertensive and who have been taking an oral contraceptive for there to be a high suspicion that the two are related.

11.5

There are several groups of women to whom oral contraceptives should be given with caution, including women over 40 years, those with a family history of premature CHD, and those who are heavy cigarette-smokers (more than 20 a day) or have other risk factors. The combination of several of these factors is particularly liable to carry an increased risk of myocardial infarction when an oral contraceptive is used.

11.6

All women being considered for an oral contraceptive should have their blood pressure measured. In women with a family history of CHD or diabetes mellitus, the plasma lipids should be determined.

12. OTHER FACTORS

12.1 *Dietary Fibre*

1. There is considerable interest in the role of dietary fibre ("unavailable carbohydrate") ranging from the extreme view that CHD is due to a deficiency of dietary fibre to the more modest claim that it is a factor in lipid metabolism. Chemically, dietary fibre is made up of cellulose, hemicellulose, pectin materials and lignin. Fibre has the general properties of holding water, exchanging cations and absorbing bile acids and each of its chemical constituents has these properties to a varying degree. There is also a complex relationship between the bacteria that hydrolyse fibre and the effect of this process on the properties of fibre.

2. By altering colonic metabolism, dietary fibre has the potential to affect fat metabolism, bile characteristics, liver metabolism, the toxicity of drugs and faecal characteristics. However, wheat fibre appears to have no consistent effect on plasma cholesterol or triglycerides in man, but there may be effects that are mediated by mechanisms other than the plasma lipid concentrations. At present the only proven role for fibre in clinical practice is in the colon by increasing fecal weight and helping in constipation and diverticulitis.

12.2 *Sugar*

1. On the basis of evidence derived from historical and epidemiological sources, from dietary histories in survivors of myocardial infarc-

tion, and from experiments in man and animals, it has been suggested that a high consumption of sugar (sucrose) is an important factor in the causation of myocardial infarction and in peripheral arterial disease.

2. While it is true that there is a positive correlation between the death rate from CHD and sugar consumption per head of population in many countries, it must be noted that sugar consumption is strongly correlated with saturated fat consumption in these countries and also with cigarette smoking. In addition, the incidence of CHD is fairly low in many countries with a high sugar consumption, e.g. in the Caribbean, Venezuela and Mauritius.

3. Sugar does not raise the plasma cholesterol level of man, although large amounts may do so in some experimental animals. In many individuals a high sugar intake can certainly raise plasma triglyceride levels and a reduction in sugar intake can lower plasma triglyceride levels.

4. At present, there is no firm evidence linking intake of dietary sugar and CHD and most workers do not regard a high intake of sugar by itself as an important factor in the aetiology of CHD.

5. Sugar is, however, an important source of calories and thus may contribute to obesity. Obesity, in turn, is associated with an increased frequency of diabetes mellitus, hypertension and physical inactivity and with raised levels of plasma triglycerides.

12.3 Coffee

1. In a large multicentre retrospective study in the U.S.A. it was found that patients surviving a myocardial infarction had consumed more coffee than matched controls. The results could not be explained by other factors such as sugar intake, smoking or occupation.

2. Four prospective studies in the U.S.A. have failed to confirm an association between the amount of coffee consumed and CHD. In one of these studies, the significant increase in "deaths from all causes" among coffee drinkers could be accounted for by the association between coffee consumption and cigarette smoking.

3. There is at present no firm evidence that coffee drinking is a factor in the development of atherosclerosis or CHD. None of the studies mentioned has considered the possible effects of coffee intake on the course of existing cardiovascular disease and no conclusions can therefore be drawn regarding this aspect of the problem.

12.4 Alcohol

There is no evidence to suggest that alcohol is a cause of CHD nor that it protects against the development of CHD. However, alcohol is a potent source of energy and even in moderate amounts taken regularly may considerably increase the total caloric intake. Generous intakes of alcohol may lead to hypertriglyceridaemia and in some persons even relatively small amounts increase the plasma triglyceride levels. The effects of alcohol in contributing to excess weight and to hypertriglyceridaemia could thus be of some indirect importance. In addition, heavy alcohol intake is often associated with increased cigarette smoking, particularly at younger ages.

12.5 Salt

1. Salt (sodium chloride) intake has not been invoked as a direct causal factor in CHD but there has long been considerable interest in the relationship between salt intake and hypertension. This interest

derives from dietary studies in human subjects (e.g. the Kempner rice diet), from animal experiments and from epidemiological observations. In general, countries with high salt intakes have a high frequency of hypertension and countries with low salt intakes have a low frequency of hypertension and the blood pressure levels in the latter do not rise with increasing age. These low intakes of salt are compatible with vigorous physical health.

2. At present we have no evidence that a reduction in the salt consumption of the whole population in the United Kingdom would widely lower blood pressure levels and thus affect the incidence of CVD and CHD. However, we agree with the recommendations made in the DHSS Report on Present-Day Practice in Infant Feeding that mothers be advised not to add salt to the solid foods in an infant's diet and that manufacturers should exercise caution in the addition of salt to their infant food products.

12.6 Water hardness and other mineral factors

1. In the United Kingdom, death rates from cardiovascular disease are higher in areas with a soft water supply and lower in those with hard water. Cardiovascular disease mortality is low in the south-east of England where water is predominantly hard and high in the north and to the west, where drinking water is predominantly soft; the mortality rates are about 40 percent higher in very soft water towns compared with very hard water towns. There is no claim made that the mineral content of drinking water is the major determinant of cardiovascular disease in the United Kingdom or elsewhere but only that there may be an important relationship between the hardness of drinking water and the regional variation in the frequency of heart attacks and strokes.

2. The strongest association between CVD mortality and known substances in the water supply is with calcium. However, soft waters, being more acid, are likely to dissolve potentially toxic trace elements from soils or from distribution systems, and several trace elements are suspected of being involved in CHD, e.g. lead, cadmium and chromium. Although there is some evidence concerning the relationship between cadmium and hypertension there is at present no firm evidence linking trace elements in drinking water to CHD.

3. Despite the strength of the statistical association between water hardness and cardiovascular mortality in the United Kingdom, we do not know that this relationship is a direct and causal one. If there is a "water factor" its identity and its mechanism of action are not known. Nevertheless, the association is a very strong one and it would therefore seem prudent in the present state of our knowledge not to soften public drinking waters unless there is some overwhelming reason for doing so and then only to do so moderately. Where domestic water softeners are used, it might be prudent for drinking water to be taken from the mains supply.

13. CHILDREN

13.1 Introduction

In this section we are concerned with primary prevention as it applies to children before puberty. Children should be considered in relation to their families and in practice the stimulus for preventive measures in children will usually be the occurrence of a CHD event or a stroke in one of the parents. Since the pathological changes in blood vessels that will ultimately progress to atherosclerosis almost certainly start

in childhood, measures designed to prevent or delay their development should apply as much to children as to adults. All of the major risk factors identified in adult life (hypercholesterolaemia, hypertension, physical inactivity and cigarette smoking) can occur during childhood, and obesity is common. Doctors and others concerned with the care of children should be actively concerned with the prevention and management of these factors.

13.2 Plasma cholesterol

Hypercholesterolaemia is the only common type of hyperlipidaemia in childhood. The level at birth is around 80 mg/dl, whatever the ethnic origin or country of residence of the parents or the mother's plasma cholesterol level. During the first year of life concentrations rise rapidly and are markedly influenced by the type of milk fed to the baby. Breast fed babies have, on average, the highest levels, and those fed artificial formulas with a high content of polyunsaturated fat (linoleic acid) have the lowest levels. By one year of age, the cholesterol level shows no significant relationship with either the level at birth or with the type of milk feeding in the early months of life. After the age of one year cholesterol levels show little change throughout the remainder of childhood, but mean concentrations vary between populations in a manner similar to that observed in adults, i.e. higher values are found in industrialised countries.

13.3 Familial hypercholesterolaemia

1. Familial hypercholesterolaemia (familial hyperbetalipoproteinemia, Type II) is clearly manifest in affected children after the age of one year. Although it could probably be diagnosed at birth in children from affected families by complicated techniques, there seems little advantage in starting treatment for the heterozygous form during the first year of life and diagnosis should be delayed until about one year of age.

2. In families known to have or suspected of having this disorder, investigation of the children is justified, but population screening for hypercholesterolaemia either at birth or later in childhood is not indicated (Fig. 16). There may be difficulties in interpreting borderline plasma lipid levels because of lack of data on normal values in childhood. In doubtful cases, children should, if possible, be referred to centres with special experience of lipid abnormalities in this age group.

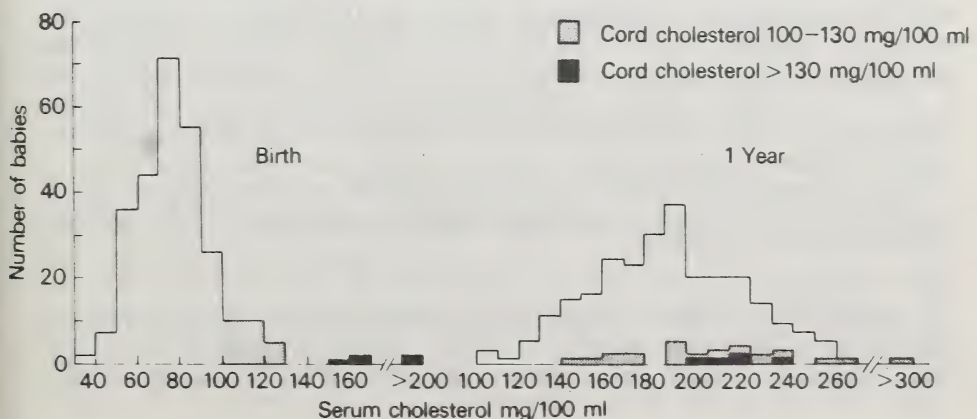


FIGURE 16.—Serum cholesterol concentration in 271 babies at birth and at one year (Darmady *et al.*, 1972).

3. General dietary advice given to adults which aims to lower plasma cholesterol concentration by reducing the amount of saturated fat eaten by partial substitution with polyunsaturated fat can just as well be followed by children over the age of one year. In young babies, however, there is no evidence to justify the promotion of milks rich in polyunsaturated fat as measures to prevent the early development of atherosclerosis.

4. In children in whom the diagnosis of familial hypercholesterolaemia has been established and who have a family history of early CHD, treatment should probably be started as soon as the diagnosis is made. Dietary treatment is likely to be effective only in a minority of children (about 20 percent) in the long term and drugs such as cholestyramine will be necessary for the remainder.

13.4 Blood pressure

1. Hypertension is rare in childhood. Blood pressure measurements are not often made as a routine and results are often inaccurate. Epidemiological studies have shown that higher blood pressures found in children will persist as they grow older, and that those with hypertensive parents are also likely to have higher than average blood pressure.

2. It is not known whether a high sodium intake in infancy influences the blood pressure of children. Babies fed on artificial formulae based on cows' milk take in more sodium than those fed on human milk, and the total salt intake is further increased when solid foods are introduced. High sodium intakes in the early months of life have no nutritional value, have adverse effects such as hypernatraemia, and should for these reasons alone be discouraged.

13.5 Cigarette smoking

1. A few children start smoking by the age of ten and smoking is frequent by the age of 15 years. Children tend to copy the smoking habits of their parents and older brothers and sisters.

2. Doctors, other health workers, and teachers should take all possible steps to discourage the smoking habit, by example, advice and encouragement. Parents should be told how smoking may affect their children's health and that the best positive action they can take is to stop smoking.

13.6 Physical inactivity

1. Although it is assumed that all children are by nature physically active, the present-day sedentary habits of adults have to a large extent spread to children. One study in the U.S.A. showed that adolescent girls spent less than one hour of the day occupied in strenuous or moderate activity and most of the waking hours were spent sitting in transport going to school, sitting at school or sitting at home watching television.

2. Parents should encourage their children to have regular daily exercise or to play games and the suggestions on page 774 for adults apply equally to children.

13.7 Obesity

1. Obesity is the most common nutritional disorder of childhood in industrialised societies. Studies of its prevalence are, however, scanty and hampered by lack of an agreed definition. Nevertheless, about 25

to 30 percent of babies are overweight during the first year of life, about 2 to 6 percent of primary school children are obese, and at puberty the incidence rises sharply, particularly among girls. The prevalence of obesity appears to have increased in adolescent girls over the past two decades.

2. Obese children are likely to become obese adults. The vast majority (80 percent) of obese children referred to hospital clinics for treatment subsequently relapse. The long-term significance of obesity in babies needs further study; most fat babies are of normal weight at school entry, but whether over-nutrition in the early months of life has a more subtle and permanent effect on weight regulation in later life is not known.

3. It is highly desirable to prevent obesity. Measures that can be adopted in childhood are—

(a) better education in general nutritional principles for parents (including parents-to-be, i.e. school children of both sexes), doctors, health workers and teachers;

(b) better instruction for mothers in infant feeding, including active promotion of breast feeding;

(c) assessment of nutritional status at infant and school clinics by weighing and skinfold measurements, with action at the first evidence of excessive fatness.

13.8 Combined risk factors

1. In children, as in adults, risk factors may occur in combination and, as for adults, risks are likely to be similarly increased.

2. Obese children may have above-average blood pressure and plasma cholesterol levels.

3. For children in whom one major risk factor has been identified, e.g. familial hypercholesterolaemia, special attention should be paid to the prevention of other factors such as obesity and cigarette smoking.

13.9 Conclusion

Children should not be regarded in isolation from their families. Risk factors that operate in adults may equally operate in children and similar measures for their control are indicated.

14. THE ROLE OF GENERAL PRACTICE

14.1 Introduction

1. The prevention of CHD in the community is predominantly the role of the general practitioner, and the Working Party considers that the continuation and extension of good general practice should provide the main means of identifying high-risk subjects.

2. Mass screening for CHD and its associated risk factors is not recommended (see 14.6). An increased awareness in general practice of the usefulness of identifying risk factors would probably make, at relatively low cost, a much greater contribution to the control of CHD than centralised screening programmes.

3. The evidence that the occurrence of a number of risk factors in the same individual increases the chance of myocardial infarction or sudden death is sufficient to justify an attempt to identify such individuals and to reduce their risk. Because risk factor reduction frequently involves alteration in behaviour, e.g. smoking, exercise, diet,

and may involve drug treatment for hypertension, both advice and treatment should be given by an individual physician to an individual patient. The general practitioner is particularly well placed both to identify those at high risk and to help them to reduce their risk. In many practices the process of identifying and advising individuals at high risk of disease is an accepted part of good medical management and the recommendations made in this section are designed to encourage what is already being done and to further promote the best use of existing facilities in the prevention of CHD.

14.2 Existing facilities and the identification of those at high risk

In any one year about 60 percent of registered patients between 25 and 65 years of age consult their general practitioner and within five years most, although not all, will have had occasion to see him. For all these patients there are records which frequently include (or could include) data regarding family history, occupation, smoking, exercise, blood pressure and weight. Thus, most of the known risk factors are easily identified and then it only remains to decide which groups of individuals require further investigation such as determination of blood lipids. At present, blood pressure seems the physical measurement with the best potential for prevention of stroke and, although the effect of blood pressure reduction on the incidence of CHD has not yet been determined, the blood pressure can be regarded as the key index for identifying high risk of CHD in the apparently healthy population. Whatever the patient's reason for attending the doctor, the opportunity should be taken to ensure that the blood pressure has been measured and recorded at least on one occasion.

14.3 Selective health examinations

1. There are certain special groups in which a health examination should be carried out—

(a) Those with a strong family history of cardiovascular disease (heart attacks, sudden death, angina pectoris, stroke, peripheral vascular disease, hypertension).

(b) Children and siblings of people manifesting CHD under 50 years of age, and of CHD patients investigated in hospital and found to have hypercholesterolaemia (in the region of 275 to 300 mg/dl (7.1 to 7.8 mmol/litre)) or above.

(c) Children and siblings of persons with familial hyperlipidaemia, whether or not CHD has become manifest.

(d) Those in whom several risk factors are found to be concurrently present, e.g. patients who have a family history of CHD or stroke and who have even moderate hypertension, smoke cigarettes, are overweight and/or have glucose intolerance/diabetes mellitus.

(e) We do not recommend members of the public to present themselves to their doctors for routine screening for CHD risk factors. However, some individuals are particularly concerned about their risk of CHD and will request a health examination. These individuals should be offered limited and discretionary use of risk factors screening because they represent a highly motivated group likely to comply with treatment and advice on behaviour. Many of these patients may already have been informed about their risk factor status through participation in a health screening programme (commercial, industrial or research).

2. The primary objective in the selective health examination is to detect symptomless persons at high risk of CHD and to offer them advice or treatment. In these subjects a record card with details of sex, age, occupation, height, weight, blood pressure and family history should be completed and a fasting blood sample obtained for plasma lipid estimation. Glucose tolerance tests are not routinely indicated except in those who are the children of diabetic subjects. In all these groups the general practitioner is ideally placed to give advice and to modify the pattern of treatment and surveillance according to the needs of the situation as indicated by the results of the examination.

Examination of these individuals combined with attention to the behavioural problems of smoking, diet and obesity and to the medical problems of hypertension and hyperlipidaemia could contribute to the primary prevention of CHD. It might also be the most reasonable and practical approach to the prevention of further episodes in those who have already manifested the disease. Where such programmes make provision for evaluation, a useful contribution could be made to our knowledge of the effectiveness of preventive procedures.

14.4 Electrocardiography/radiography

Currently we lack evidence that detection of electrocardiographic abnormalities leads to action that will improve prognosis, although many abnormalities are important in the assessment of CHD risk. Many practices now possess their own electrocardiograph and have access to chest radiography facilities but there is no need to undertake these examinations routinely in apparently healthy subjects who are being examined for the presence of CHD risk factors. Electrocardiographic examination, however, plays an important part in the assessment of hypertension and the diagnosis of chest pain. Recognition and interpretation of specific abnormalities requires good apparatus, good technique and special experience and, where uncertainty exists, the services of specialised departments should be sought.

14.5 Research and extension of existing facilities

The Working Party considers that general practice should be the main mechanism for identifying high-risk subjects in the community and that GPs should further develop the use made of the information coming before them. This continuation and extension of good general practice could produce a clearer picture of CHD risk in the community. However, practices differ considerably in their structure and facilities and the following suggestions are intended only as a guide to possible developments. They mainly concern routine health examinations that carry no promise of benefit from treatment and are only an extension of good clinical practice into the field of early detection and prevention of disease.

(a) It should be possible, using receptionists, practice nurses or medical auxiliaries, to introduce a scheme of surveillance into those general practices where no such schemes exist, and which possess average facilities. The basis would be a record card containing information on (i) sex (ii) date of birth (iii) occupation (iv) height (no shoes) (v) weight (indoor clothes) (vi) blood pressure (vii) smoking status (viii) family history. This could be completed by a medical auxiliary at least once in respect of all patients aged over 40 years in the practice list, making use of the opportunities afforded by visits to the general practitioner for any reasons whatsoever.

(b) More advanced but still limited schemes of health examination could be introduced into general practice, especially by interested practitioners working together in health centres where auxiliary help is available. An age and sex register identifies the population at risk and allows reliable estimates to be made of rates of response and of the prevalence and incidence of illness and death.

(c) Examination of new list patients should be encouraged where this can be done within the framework of (i) and (ii) above.

14.6 *Mass screening for CHD risk factors*

Current trials and studies have yet to define the appropriate role of screening in the health of the community but the Working Party considers that mass screening for CHD and its associated risk factors should not be introduced for the whole population at the present time. The known risk factors for CHD—hypertension, cigarette smoking, raised plasma lipid levels, obesity and physical inactivity—occur in the community with such high frequency that there are formidable practical implications for resources if all precursors of CHD were to be detected and advice and management offered to all persons at risk. In addition, many of the “abnormalities” cannot be adequately defined, e.g. hypertension, hypercholesterolaemia, physical inactivity, and so the sensitivity and specificity of the tests to determine “abnormality” are low. To these considerations must be added the uncertainty regarding the effectiveness of intervention.

Mass screening remains a valuable tool for epidemiological research, for deriving rates of disease and predisposing factors in the community and for conducting large-scale field trials of interventive advice or treatment.

14.7 *Conclusion*

Although the difficulties are formidable and the outcomes uncertain, the present epidemiological situation in CHD would seem to indicate the need to encourage the present trend in good medical practice of identifying those at high risk and offering them advice or treatment whenever this can be achieved without detriment to existing practice and services.

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16. APPENDICES

16.1 Plasma lipids

Cholesterol and triglycerides are transported in the plasma bound to proteins in the form of lipoproteins. Plasma lipoproteins have been classified according to their chemical composition and the related density, their behaviour when exposed to electrophoresis and their particle size.

A major problem in lipoprotein classification arises from their interconvertibility. It is better to think of the lipoproteins as a dynamic system of interchangeable cholesterol and triglycerides bound to protein, rather than as discrete and constant lipoprotein molecules. It is also essential to remember that the usage of lipoprotein classifications relates to the plasma and not the patient and that there is only a limited relationship between plasma lipoprotein patterns and the underlying pathogenesis. Further, it is established that more than one aetiology may be responsible for a given lipoprotein pattern.

Figure 17 illustrates the continuity between lipoprotein classes with regard to lipid composition and shows how the plasma lipoproteins are classified according to various methods of biochemical analysis (ultracentrifugation, paper electrophoresis, nephelometry). The two groups of lipoproteins that at present are considered to be more relevant to CHD are—

1. *Low Density Lipoproteins* (LDL; beta lipoprotein).—These are rich in cholesterol. An increased concentration of LDL may be referred to as Type II (Frederickson). For the purposes of this report an increased concentration of LDL is referred to as hypercholesterolaemia. In the Frederickson classification, Type IIA refers to elevation of plasma cholesterol alone; Type IIB refers to an elevation of both plasma cholesterol and triglycerides.

2. *Very Low Density Lipoproteins* (VLDL; pre-beta lipoprotein).—These are proportionately rich in triglycerides. An increased concentration of VLDL may be referred to as Type IV (Frederickson). For purposes of this report, an increased concentration of VLDL is referred to as hypertriglyceridaemia. For the assessment and management of the majority of individuals, estimation of plasma cholesterol and triglycerides is all that is necessary.

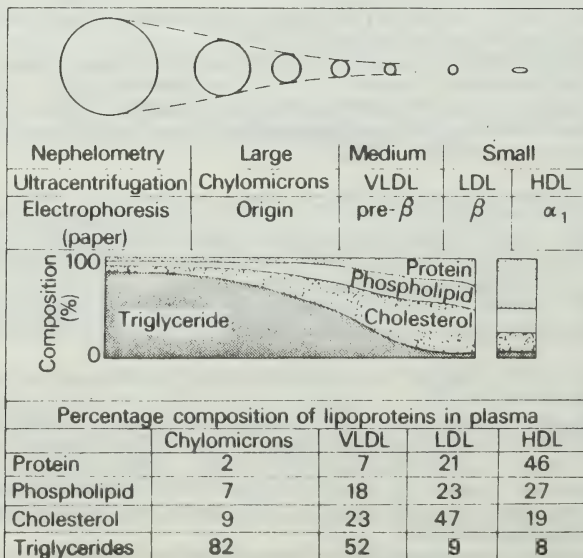


FIGURE 17.—Lipoproteins in plasma: a comparative view of ultracentrifugation, paper electrophoresis and nephelometry with the percentage composition of the various lipoproteins in plasma.

16.2 Dietary fats

The housewife who buys butter, margarine or lard knows what she means by "fat." Cooking oil is a liquid fat. Table fats, cooking oil and the fat on meat are visible fats but there is non-visible fat in most other foods as well, ranking from nearly 40 percent in many cheeses, potato chips and chocolate down to only a trace in most fruits and vegetables. The biochemical term "lipid" covers all the chemical substances included in the housewife "fat", such as triglycerides, cholesterol and phospholipids. Cholesterol is present in a number of foods (eggs are the chief source) but it is only a small part of the average dietary fat intake.

The form in which fats chiefly occur both in foods and in the fat depots of the body is the triglycerides composed of fatty acids and glycerol. There are over 40 fatty acids found in nature, accounting for the diversity and specificity of the natural fats. The fatty acids are made up of carbon, hydrogen and oxygen and their properties depend upon the length of the carbon chain and the ability of the carbon chain to combine with additional hydrogen atoms. This latter ability is referred to as the degree of saturation or unsaturation. Fatty acids are classified as saturated, mono-unsaturated, and polyunsaturated. Saturated fatty acids contain as many hydrogen atoms as the carbon chain can hold, e.g. palmitic and stearic acids. Mono-unsaturated fatty acids have two hydrogen atoms missing in the carbon chain, i.e. one double-bond linkage is available; oleic and palmitoleic acids are examples. Polyunsaturated fatty acids (PUFA) may have 2, 3 or 4 more double-bond linkages available, i.e. 4, 6, 8 or more hydrogen atoms are missing in the carbon chain. Examples are linoleic acid (2 double-bonds), linolenic acid (3 double-bonds) and arachidonic (4 double-bonds).

The ratio of dietary polyunsaturated to saturated fatty acids is often abbreviated to the P/S ratio.

Fatty acid composition of food

All the fat-containing foods in our diet consist of a mixture of fatty acids and one should not think of any particular food item as being purely saturated, mono-unsaturated or polyunsaturated. Most foods can, however, be classified as predominantly saturated, mono-unsaturated or polyunsaturated. Saturated fatty acids comprise about 50 percent of the fatty acids contained in the average British diet and provide about 21 percent of total energy intake. These are principally the solid fats of animal origin such as those in milk, butter and meat. Some plant products (chocolate and coconut) contain large amounts of the saturated fatty acids. The predominantly unsaturated vegetable and plant fatty acids that have been hardened by hydrogenation become saturated fatty acids. Saturated fatty acids in the diet increase the plasma cholesterol concentration.

Mono-unsaturated fatty acids comprise about 40 percent of the fatty acids in the average British diet and provide about 16 percent of the total energy intake. The best example is oleic acid, found in appreciable amounts in most foods. Oleic acid comprises nearly 50 percent of the fatty content of bacon and about 75 percent of the fatty acid content of olive oil. These fatty acids have little effect on the plasma cholesterol concentration.

Polyunsaturated fatty acids (PUFA) in the average British diet are much less in quantity than either the saturated or mono-unsaturated fatty acids and they provide slightly less than 5 percent of the total energy intake. Corn oil and sunflower oil are among the richest food sources of this group of fatty acids. Chicken, fish and many nuts (excluding coconut) are good sources of PUFA. The polyunsaturated fats in the diet tend to lower the plasma cholesterol concentration.

Dietary cholesterol is only a part of the body's supply of cholesterol which is derived in two main ways: by synthesis in the tissues, particularly the liver and intestinal wall (endogenous cholesterol) and from the diet (exogenous cholesterol). The body synthesis of cholesterol is several times greater than the dietary intake. There is a feedback mechanism by which the intake of dietary cholesterol can suppress endogenous cholesterol synthesis but there is considerable variation in this mechanism from one individual to another and possibly from one race to another.

The average British diet contains about 500 mg of cholesterol per day of which 40 to 60 percent is retained in the body. With higher intakes of cholesterol the percentage absorption falls. The type of dietary fat that accompanies the cholesterol may be a factor in determining the absorption of cholesterol. Fats tending to elevate the plasma cholesterol are the ones in which dietary cholesterol is most soluble. The major dietary sources of cholesterol are egg yolk, liver and kidney. Food from plant sources contains no cholesterol.

Table 6 shows the daily nutrient content and the energy value of the average British diet. Table 7 shows the sources of fat in the average British diet, with major contributions from butter, margarine, cooking fats and meat.

TABLE 6.—NUTRIENT CONTENT AND ENERGY VALUE OF HOUSEHOLD FOOD

	Number	Percentage total calories
Energy kcal.	2,400	-----
Protein g.	71	12
Carbohydrate g.	293	46
Fat g.	111	42
Saturated.	52	21
Monounsaturated.	42	16
Polyunsaturated.	12	5
Cholesterol mg.	500	-----

Source: National Food Survey 1973.

Table 7.—Sources of fat (percent) in the British diet.

	Percent		Percent
Butter, margarine and other fats.---	35	Poultry -----	1
Milk and cream.-----	15	Fish -----	1
Cheese -----	4	Cakes and biscuit.-----	6
Eggs -----	3	Other foods.-----	7
Meats -----	28		

Source: National Food Survey 1973.

For more detailed information on dietary components refer to Human Nutrition and Dietetics, 6th edition by Davidson, Passmore, Brock and Truswell Churchill-Livingstone, 1975.

16.3 Suggestions for exercise

Introduction. Young children should be encouraged to take an interest in games or other physical activities that can become part of their lifetime pattern of behavior. For middle-aged people who have not taken any regular exercise for many years, there are no risks in regular dynamic exercise as long as the programme begins gently and increases in vigour only gradually. Most people do not need a medical examination before starting an exercise programme. Older persons, the obese and those with a history of cardiovascular disease or symptoms should first consult their doctor. Those who develop unexpected symptoms during exercise should also seek medical advice.

1. Simple "keep-fit" exercises twice a day using the main muscle groups in turn, but if unaccustomed to exercise, not the same ones on consecutive days.

2. Walking on the level at ordinary pace (3 mph/4.2 kph) and gradually increasing the distance, the pace and the slope. Most people could walk at least part of the way to work, to a further bus stop, to the station, or after parking the car.

3. Every opportunity should be taken to climb stairs.

4. Vigorous exercise in some form can be undertaken at the weekends or on holidays and, if possible, also during the week. Exercising as a family or with a friend is likely to increase enjoyment and persistence. Jogging and running are probably the most efficient means of getting brief vigorous exercise at low cost.

5. Getting breathless some time every day is a good habit however it is achieved e.g. running, cycling or climbing stairs.

6. Frequency and duration. Exercising twice a week, preferably not on consecutive days, appears necessary to retain most of the physiological adaptation of improved performance. A minimum of 15 to 30 minutes of vigorous exertion appears to be indicated for both physiological and preventive effects.

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Professor H. Keen and Dr. R. J. Jarrett of the Unit for Metabolic Medicine, Guy's Hospital Medical School, London, contributed the draft section on diabetes mellitus, Dr. H. Tunstall Pedoe, Epidemiology Dept., St Mary's Hospital Medical School, London, provided information on community aspects of coronary heart disease. The draft dietary recommendations were prepared by Miss Jean Marr, Department of Clinical Epidemiology, Royal Free Hospital School of Medicine, London.

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D.

**A BENCHMARK SURVEY OF
ISSUES RELATING TO FOOD NUTRITION
AND THE AMERICAN CONSUMER**

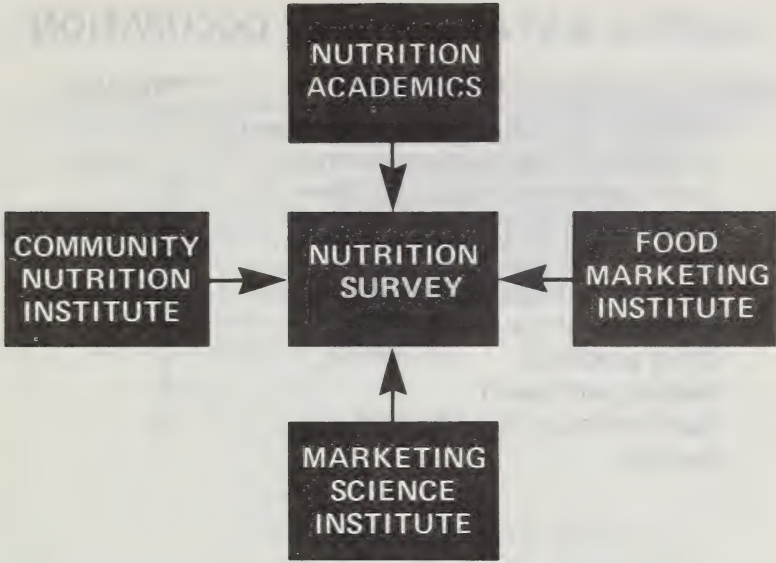
Conducted by the **Marketing Science Institute**, Cambridge Massachusetts
with grant support from **Family Circle Magazine**

Alden G. Clayton, MSI

John A. Quelch
University of Western Ontario
and MSI Research Associate

OBJECTIVES

- Survey groups interested in nutritional well-being of U.S. consumers on:
 - Barriers
 - Potential Solutions
- Establish areas of relative agreement and disagreement
- Benchmark data for larger survey

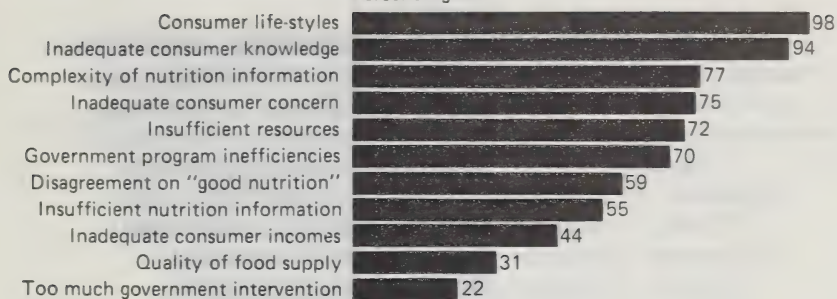


SAMPLE BREAKDOWN BY OCCUPATION

	Percentage
Nutritionist or dietitian (government)	20
Government program administrator	13
Employee of food manufacturer	12
Consumer activist	10
Other	10
Nutrition science academic	9
Employee of food retailer	7
Other academic	7
Nursing profession	5
Nutritionist or dietitian (industry)	4
Farmer	2

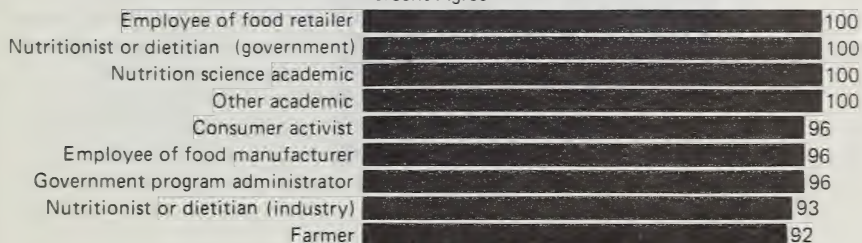
BARRIERS

Percent Agree



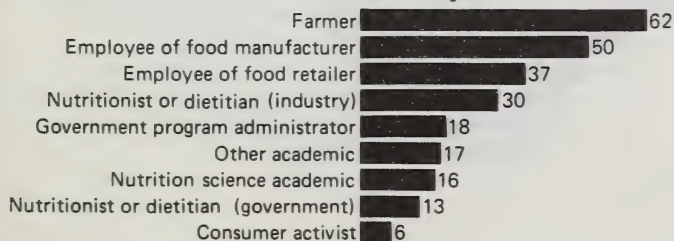
CONSUMER LIFE-STYLES

Percent Agree



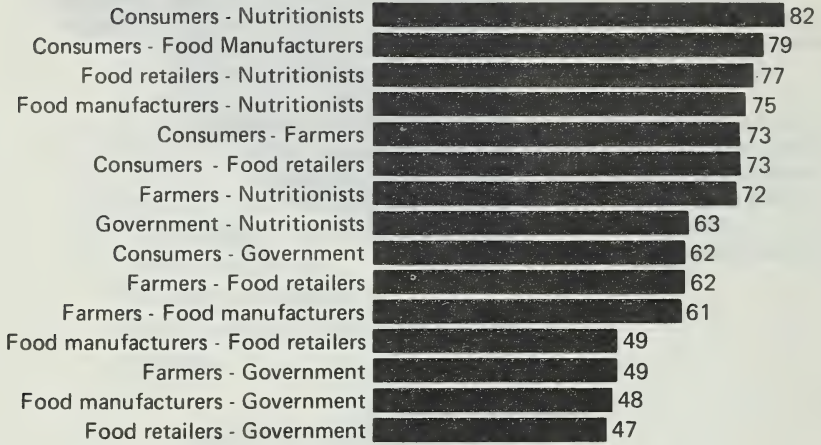
TOO MUCH GOVERNMENT INTERVENTION

Percent Agree



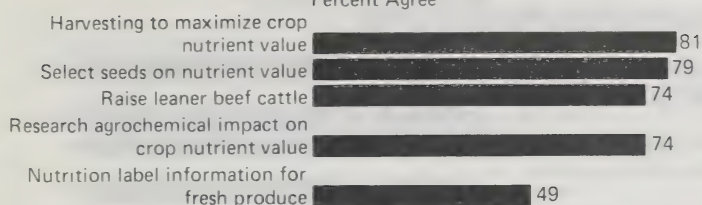
NOT ENOUGH COMMUNICATION

Percent Agree



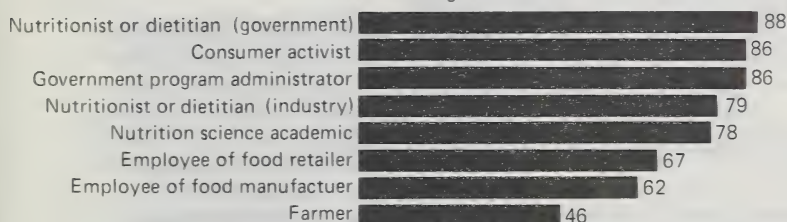
ACTIONS BY FARMERS

Percent Agree



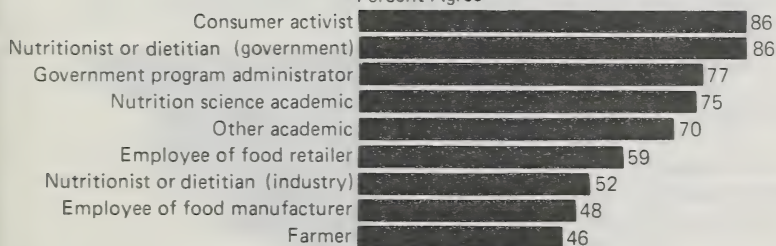
HARVESTING TO MAXIMIZE CROP NUTRIENT VALUE

Percent Agree



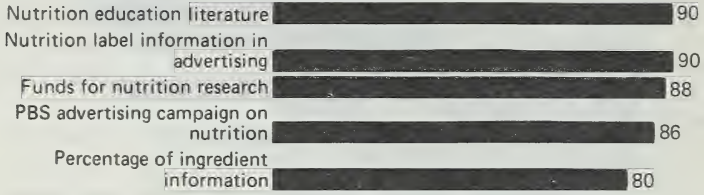
RAISE LEANER BEEF CATTLE

Percent Agree



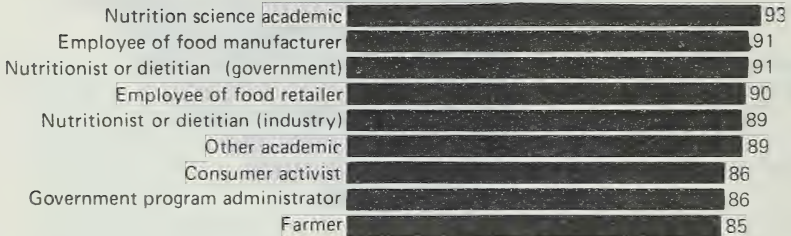
ACTIONS BY FOOD MANUFACTURERS

Percent Agree



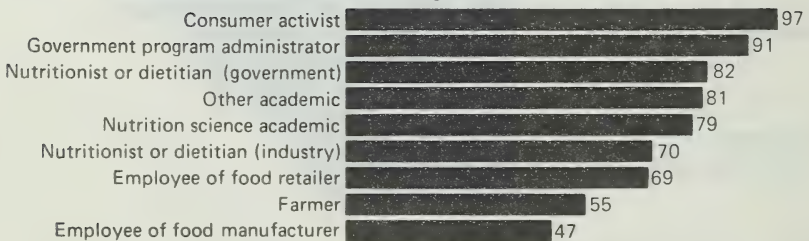
PROVIDE NUTRITION EDUCATION LITERATURE

Percent Agree



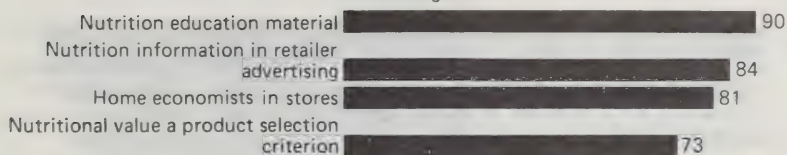
PROVIDE PERCENTAGE OF INGREDIENT INFORMATION

Percent Agree



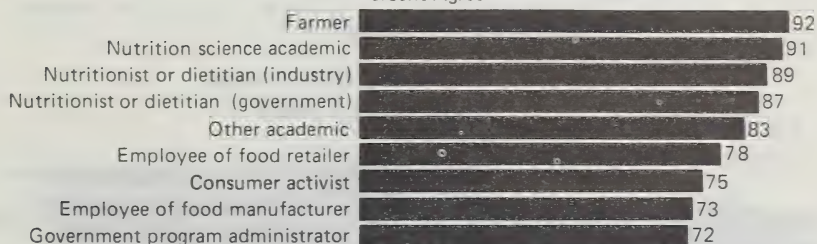
ACTIONS BY FOOD RETAILERS

Percent Agree

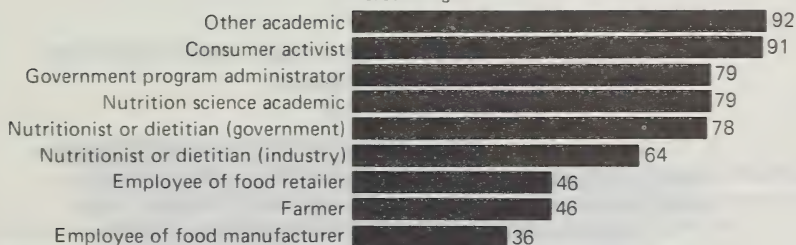


HOME ECONOMISTS IN STORES

Percent Agree

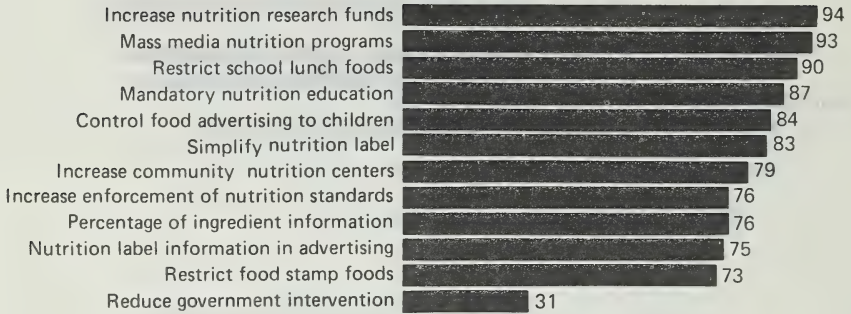
NUTRITIONAL VALUE AS A
PRODUCT SELECTION CRITERION

Percent Agree

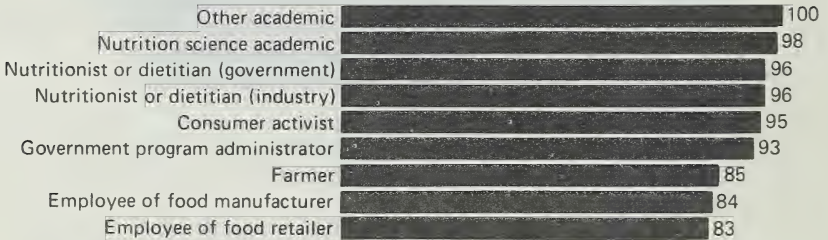


ACTIONS BY GOVERNMENT

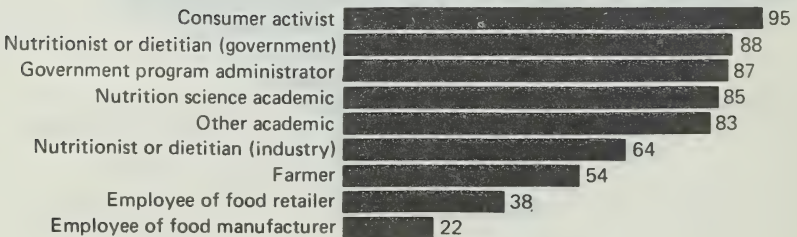
Percent Agree

INCREASE NUTRITION
RESEARCH FUNDS

Percent Agree

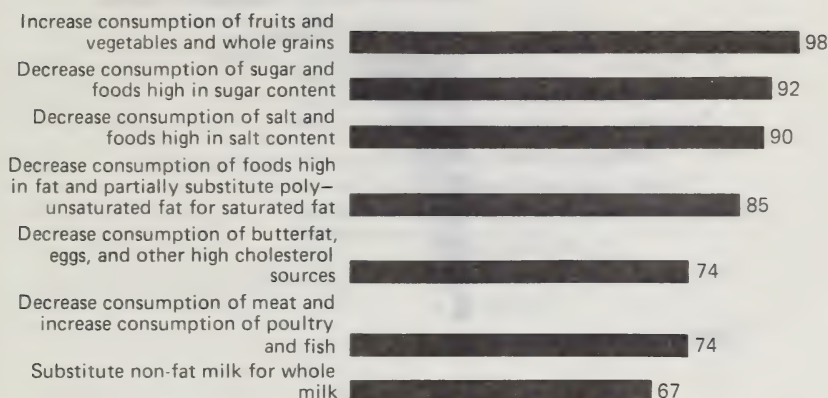
NUTRITION LABEL INFORMATION
IN ADVERTISING

Percent Agree



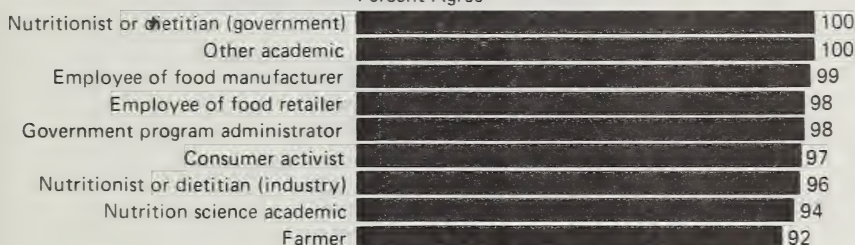
DIETARY GOALS

Percent Agree



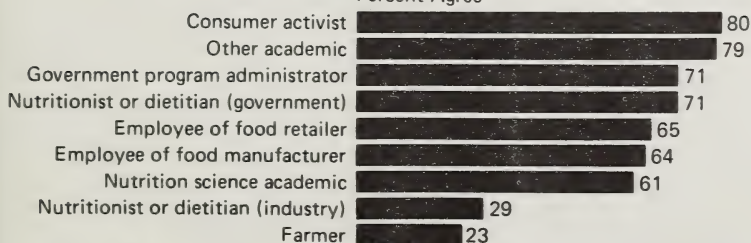
INCREASE CONSUMPTION OF FRUITS, VEGETABLES, AND WHOLE GRAINS

Percent Agree



SUBSTITUTE NON-FAT MILK FOR WHOLE MILK

Percent Agree



**DIETARY GOAL
COMMITTEE MEMBERSHIP**

Average percentage

Nutritionists / Dietitians	20
Nutrition scientists	18
Consumer organizations	13
Medical profession	11
Food manufacturers	9
Government agency officials	8
Food retailers	7
Government legislators	6
Other	3
"Distinguished Americans"	2

AREAS OF MOST AGREEMENT

- | | |
|---------------|---|
| Barriers | Consumer life-styles
Inadequate consumer knowledge |
| Actions | Increase nutrition research funds
Mass media nutrition programs
Nutrition education literature
Restrict school lunch foods |
| Dietary goals | Increase consumption of fruits and vegetables and whole grains
Decrease consumption of sugar
Decrease consumption of salt |

AREAS OF MOST DISAGREEMENT

- | | |
|---------------|--|
| Barriers | Inadequate consumer incomes
Insufficient nutrition information |
| Actions | Nutritional value a product selection criterion
Percentage of ingredient information
Raise leaner beef cattle
Reduce government intervention |
| Dietary goals | Decrease consumption of butterfat, eggs, and other high cholesterol sources
Decrease consumption of meat and increase consumption of poultry and fish
Substitute non-fat milk for whole milk |



E. Report No. 32 to the Storting
(1975—76)

**On Norwegian
nutrition and food policy**

Report No. 32 to the Storting

(1975—76)

On Norwegian nutrition and food policy

*Recommendation of 7. November, 1975 from the Ministry of Agriculture,
approved by Royal Decree of the same date.*

(Presented by Mr. Thorstein Trøholt, Minister of Agriculture).

Chapter 1. Summary of the Governments Proposals and Evaluations Concerning Norwegian Nutrition and Food Policy

1.1 INTRODUCTION

It is the Government's view that the nutrition and food policy should coordinate several important objectives and considerations. These may be summed up as follows:

1. Healthy dietary habits should be encouraged.
2. A nutrition and food policy should be formulated in accordance with the recommendations of the World Food Conference.
3. For reasons connected with the question of supply, the policy should aim at increased production and consumption of domestic food and at strengthening the ability to increase rapidly the degree of self-sufficiency in the food supply.
4. For regional policy reasons the highest priority should be placed on utilizing the food production resources in the economically weaker areas.

A primary task of the future nutrition and food policy will be an active coordination of these considerations.

The relationship between nutrition and health is discussed in Chapter 2. It is stressed here that the prerequisite for proper nutrition of the population is to have enough food, in order to be able to satisfy the need of both a sufficient energy supply and a sufficient supply of the necessary nutrients. Scarcity of food is the main problem facing the majority of the world population, as has also sometimes been the case in our own country.

In Norway (as in other western industrial-

ized countries) the course of development since the turn of the century has resulted in food having become more plentiful and a greater variety of foods has become available to the population. This in turn has led to improved nutrition with a better supply of essential nutrients. Furthermore, during this period, there has also been a considerable improvement in the general state of health (measured in terms of infant mortality, growth and development of children and youth, resistance to infectious diseases, etc.). There is no doubt that this improvement is very largely due to the general diet.

However, the fact of there being enough food to provide the basis for a plentiful diet has proved in itself to be no guarantee that the diet is entirely safe from the health angle. There has been a sharp increase in the incidence of several diseases associated with nutrition in those countries where food is plentiful, and where the general standard of increase in cardiovascular diseases which is the most serious, but other trends are causing concern too.

As far as possible it is now necessary to alter the diet in order to prevent the occurrence of these diseases, while at the same time retaining the favourable features of our present diet. A healthy diet may be composed in various ways. Due regard must be paid to what is suitable, for example the aim must be a diet satisfying reasonable requirements as to taste and variety and in accordance with

what the country is capable of producing and supplying. It goes without saying that any adaption of diet will ensue from consumers voluntarily altering their dietary habits.

Taking the recommendations from the World Food Conference as a starting point, it would be right to view the nutrition and food policy in relation to the global situation as regards production and supplies. As part of solving the world's food problems, the developed countries were recommended to increase their food production and to implement measures for improving their own pattern of consumption. Such measures must, however, make allowances for the developing countries' trade interests as promoted through international organizations. These questions are discussed in more detail in Chapter 3.

Chapter 4 discusses food production and dietary trends in Norway.

The total annual fish catch in the 1970's averaged 2.7 million tons. For this period, 22—24 per cent of the catch has consisted of what is traditionally termed fish for human consumption. Approximately 90 per cent of the total catch is exported.

According to Report No. 64 to the Storting for 1963—64, agricultural production in Norway has been directed towards covering the national demand for milk, butter, cheese, meat including pork and eggs. In addition, the aim was to provide full market coverage of potatoes, berries and rough vegetables suitable for storing, such as cabbage and carrots. In respect of fruits and vegetables less suitable for storing, the goal has been the fullest possible market coverage by domestic production. In respect of grains, the established aim was to cover as large a share of the need for grain as is deemed to be warrantable. The aim has been to ensure that livestock production is as far as possible based on locally produced fodder. In general, agricultural production has followed the trends in consumption and the production goals have largely been attained.

A general feature of the trend in food consumption has been the high degree of stability. Over a period, however, for example over the past 20—25 years, changes have taken place. The percentage of food consumption represented by grain has gradually fallen to a substantially lower level. In the past few years, however, this tendency seems to have been reversed. The consumption of potatoes has dropped considerably, while the consumption of fruits and berries has shown a significant increase. Norway has a much higher consumption of fish and a lower consumption of meat than most other western industrial-

ized countries. Fish consumption has fallen considerably in recent years. Meat consumption has shown a tendency to rise throughout the period, and particularly in the last few years.

The consumption of whole milk has generally remained stable, while that of skimmed milk has increased steadily in recent years. The consumption of butter and margarine has been comparatively steady. Sugar consumption showed a rising tendency up to 1968, but has lately declined.

Over a longer period, there have been considerable changes in the diet with respect to the amount of food of vegetable origin (including cereals) compared to animal products. In 1938, vegetable products represented about 68 per cent of the energy content in the general diet. By 1968, this share has been reduced to 54 per cent. Later, the percentage of vegetable-derived food energy has again somewhat increased.

The share of fat in the total energy intake has also shown a gradual increase over the last 75 years up to now, in 1973 covering about 42 per cent of the total energy content in our diet.

The degree of self-sufficiency provides an approximate expression of the degree to which total food needs are covered by Norwegian production, and is calculated on an energy basis. In 1973, the degree of self-sufficiency of food amounted to 47.7 per cent, agricultural products constituting 30.2 per cent and fish products 7.5 per cent. If imported feed concentrates are deducted, the share of food consumption deriving from Norwegian agricultural production, based on domestic fodder, amounted in 1973 to 31.7 per cent. The reasons for the low degree of self-sufficiency are that all sugar, the major proportion of food grain and a large part of the concentrates are imported. Likewise, a considerable proportion of the raw materials for margarine and other types of fat are imported.

Chapter 6 discusses the factors influencing diet.

These factors are divided into two groups. One group includes factors not directly related to the individual consumer, for example food prices, the relation between the prices of various kinds of food, and the food available to the consumer in everyday life.

The other group of factors is more directly connected with the consumer or the household, i.e. factors such as family size and composition, the level of income, the relevant knowledge and skills, dietary pattern and preferences.

Chapter 5 includes a survey of Norwegian

food production resources and their utilization.

The area of land used for agriculture has gradually been reduced over the last 20—25 years, being 0.9 million hectares in 1974. Of this 0.5 million hectares were meadows producing hay, silage and pasture, and 0.29 million hectares were used for grain crops. The land suitable for grain production, especially for food grain, is limited. According to the Census of Agriculture for 1969 an additional area not in use of about 0.22 million hectares is suitable for reclamation.

In the Ministry of Agriculture's Division for Land Registration, a comprehensive registration of land is being carried out including, *inter alia*, new land suitable for cultivation. This registration work has not yet been completed. The Division's registrations show, however, that the total new area suitable for cultivation is considerably larger than is indicated in the Census of Agriculture. The possibilities of increasing the grain production area through bringing new areas under cultivation, are more limited, however.

With a potential annual catch of about 10 million tons, the fishing grounds in the north-east Atlantic are estimated to be the most productive, but also the most exploited fishery areas in the world. With an annual catch of 2.5—3 million tons, Norway is the most important fishery nation in these waters. In general, it would be correct to say that the present resource base in these areas limits any further expansion of fisheries.

The Government attaches great importance to measures capable of strengthening our future position in regard to supplies. It will be necessary here to strengthen the supply position in several fields simultaneously — 1) by increasing the production and consumption of domestic food, 2) by introducing appropriate storage schemes, 3) by improving import arrangements (including delivery agreements with other countries), and 4) by improving Norway's ability to increase rapidly the degree of self-sufficiency in food production. The effect of these measures must be evaluated collectively, and the effect these measures have on other fields in society must also be assessed.

An increase in food production is a necessary basis for a larger share of our food consumption being covered by Norwegian products. In this Report the main points involved in these questions are discussed.

By means of storage schemes it is possible to mitigate the effects of variations in yield levels and the effect of short-term shortages. The Government is working out plans for ex-

tending the emergency stocks of bread grain and feed concentrates. Preparatory work is also underway for expanded emergency stocks of agricultural inputs.

The organization of imports will be important for the supply situation. Delivery agreements, primarily with our neighbour-countries, may contribute to safeguarding the supply. Delivery agreements for grain have been concluded with Finland and Sweden.

Our ability to adapt consumption and production in a crisis will be decisive in assessing our supply position. These questions are being studied by a committee appointed by the Ministry of Trade and Commerce.

The Government attaches the utmost importance to the contribution made by agriculture and fisheries towards stabilizing population settlement in economically weak areas. The increase in food production should therefore mainly take place in such areas.

Changes in diet will have to be made by the individual and in the individual households. It is obvious that adjustment in the diet can only be made by consumers voluntarily changing their dietary habits. The Government's task is by various measures to encourage the desired development.

The changes aimed at deviate from the trends found today in countries with high and rising material standards.

1.2 THE GOALS OF THE NUTRITION AND FOOD POLICY

1.2.1 Relationship between Nutrition and Health

The relationship between diet and health, for instance between diet and cardiovascular diseases, is not yet entirely understood. However, there is sufficient knowledge of this relationship to recommend alterations in the diet which are desirable from the point of view of preventing these diseases.

The aforementioned unfavourable health tendencies, particularly in respect of cardiovascular diseases, as well as the gradual understanding that is being gained of the connection between nutrition and health, make it necessary for the Government to base itself on expert recommendations, issued by the National Nutrition Council, when planning Norwegian nutrition and food policy.

The Government will prepare a policy which will contribute to the following:

- The beneficial aspects of the diet are to be preserved. Conditions will be arranged so that the diet is better adapted to nutritional requirements, while general demands for taste, variety and diversity are

stressed. The different nutritional requirements of special groups such as children and young people, pregnant and breast-feeding mothers, the elderly, etc. must also be taken into consideration.

In order to obtain a better adaption of the diet to nutritional requirements it is especially important to curtail the proportion of fat in the energy supply. An objective should be to reduce the proportion of fat to 35% of the energy supply through a gradual alteration of the diet.

The decrease in the supply of fat should be replaced by foods containing starch — primarily cereals and potatoes. There should be an attempt to limit the proportion of sugar in the energy supply.

The proportion of polyunsaturated fatty acids in the total fat intake should be increased.

1.2.2 Relationship between Diet, Health and Greater Coverage of Food Consumption by Means of Norwegian Production

In the Government's view, the unreliability of food supplies and the recommendations of the World Food Conference should be met by increasing the proportion of total food consumption covered by Norwegian production, while readjusting the diet from the point of view of health.

Weighing up the pros and cons of reducing the fat content in the diet while at the same time ensuring an increase in food production is very difficult.

It is necessary to see the various sources of fat in relation to one another so that the proportion on fat in the total diet is reduced to 35 per cent of the energy content in the food. In 1973 the total content of fat from the food groups margarine, other fats, whole milk, cream, cheese, butter and meat amounted to 93 per cent of all fat.

Milk production plays an important role in our food production and a reasonable consumption of milk and milk products is desirable for health reasons. The consumption of low-fat milk should be increased considerably in comparison with whole milk, and the consumption of cream should be reduced.

The production of meat is a necessary element in the utilization of our resources. However, a continued increase in meat consumption would serve little purpose because of the desire to reduce the fat intake. On the basis of an overall view, the aim should therefore be to keep the per capita consumption of meat at about the present level.

Food production objectives make only a limited reduction in the fat consumption from milk and meat possible. If fat consumption is to be brought down to a satisfactory level from a health point of view, the consumption of margarine and of the types of fat which, in the relevant statistics, are called «other fats» must be considerably reduced.

In the production and consumption of margarine and other fats, the wish to secure a market for Norwegian-produced hydrogenated marine fat must not be overlooked, while at the same time ensuring a satisfactory composition of fatty acids. In recent years, marine fat has made up about 45 per cent of the raw material in these products. The imported vegetable fat has been about 30 per cent vegetable oils, about 15 per cent hydrogenated vegetable oils and close to 10 per cent coconut oil. Of these types of fat, vegetable oils have the most favourable composition of fatty acids, with a large proportion of polyunsaturated fat. The major proportion of the fat in hydrogenated marine fat, coconut fat and hydrogenated vegetable fat is in the form of saturated fat.

In the Government's view, the aim should be to use hydrogenated marine fat in the margarine industry to the extent that this is warranted out of consideration for a favourable composition of fatty acids in the diet. It is justifiable to replace hydrogenated vegetable fat with hydrogenated marine fat, thus bringing the amount of hydrogenated marine fat in margarine production up to 60 per cent of the raw material.

The diet must have a sufficiently high energy content. The reduction in fat must therefore be compensated, and this is best achieved by means of a considerably increased consumption of cereals, but also potatoes and vegetables. A right course will also be to increase the consumption of fish and fish products considerably. These adjustments in diet which are recommended for reasons of nutrition and health, together with the desire to increase food production, will contribute to a diet with a higher vegetable (including cereals) content.

The planned policy will lead to a reduction in grain imports. The major grain-exporting countries are the industrialized countries, while the developing countries are net importers. An increase in consumption of Norwegian food products along these lines will therefore not conflict with the interests of developing countries, as far as these have been expressed in various international organizations.

1.2.3 Increase in Consumption of Fish and Fish Products

In order to attain the goal of a substantial increase in the consumption of fish, it will be necessary to provide a greater variety of fish-based food, or food in which one of the ingredients is fish. It is therefore important to invest in research on raw materials and product development.

1.2.4 Increase in the Production of Agricultural Products

In Report No. 50 for 1974-75 to the Storting on Natural Resources and Economic Development, the Government has defined the considerations to which importance must be attached, when deciding on the size of agricultural production in our country. These may be summed up as follows:

1. Regard for the future supply situation indicates an increase in agricultural production.
2. An increase in agricultural production can contribute to stabilizing the population settlement in the areas with a weak economic base.
3. The increase in agricultural production ought to take place in such a way and at such a pace that due regard may be paid to development in other sectors of the economy.

In the Report, the Government evaluated the arguments for and against these considerations. The conclusion is that, having primarily in mind the population structure and the desire to avoid unnecessary upheaval, but also the unstable conditions in the world food market, the Government is of the opinion that there should be an increase in the production of agricultural products in Norway.

This section deals with the main developments for Norwegian agriculture towards 1990. However, the Government has neither decided on nor dealt with a comprehensive plan for agricultural development up to that time. Such a plan will be considered in connection with the ordinary long-term programme and the annual and long-term budgets. Accordingly it is clear that the Government, as well as the Storting, will have to return to these questions in these contexts. The Government wishes, however, to point out the uncertainty which is always connected with planning over such a long period of time.

The production goal for Norwegian agriculture and important elements comprised in the goal for agriculture in the context of regional

policy is evaluated in this Report. The other goals for agricultural policy and the relevant measures will be dealt with in a report on agricultural policy.

In Chapter 5 it is shown that it is possible to increase the cultivated area considerably. The possibilities of increasing grain production through cultivation of new land is, however, rather limited. The interesting question will be to what extent and how soon these resources should be taken into use within the framework of the production goals.

Both because of general national considerations and out of regard for the industry, the aim must be to secure a gradual long-term increase in production. On the basis of an overall evaluation of the various considerations, the Government has come to the conclusion that the total agricultural area ought to be increased from 0.9 million hectares in 1974 to 1.0 million hectares in 1990. The fully cultivated area should be increased from 0.79 million to 0.90 million hectares.

It is the Government's view that, on the basis of the present agricultural production goals, Norwegian agriculture should continue to cover the domestic demand for milk and milk products, cheese, butter, meat, potatoes, eggs and, as far as possible, also vegetables, fruits and berries. In respect of these products, production should be adjusted to consumption, and efforts should be made to adapt consumption according to recommendations based on supply and nutrition policy evaluations. In the case of grain, the aim should be a substantial production increase. A considerable proportion of this increase should be food grain. Increased production of berries is also desirable. In the view of the Government, sugar should not be produced in Norway.

Regional policy considerations require that the major part of the net increase in production take place in districts with a weak economic base. In 1971, 55 per cent of all agricultural land was in economically disadvantaged areas. The aim should be that up to 1990 at least the three-quarters of the net increase in agricultural area be in the economically disadvantaged areas.

The area used for potatoes, vegetables, fruits and berries needs not be increased to any great extent.

The production of roughage should be increased to somewhat above the present level. The aim will be to increase the use of roughage, and reduce the use of feed concentrates in milk production and to limit the use of feed concentrates in meat production.

Grain production plays a central role for

our food supplies. In 1975 the amount of land used for grain was 0.3 million hectares, and by far the largest proportion of grain produced was used as animal feed. In the Government's view, the aim should be to increase the grain area to 0.36 million hectares by 1990. A considerable proportion of the additional area should be used for food grain, so that the food grain crop in years with normal harvests will amount to 125 000 tons (35—40 000 hectares).

The increase in agricultural production envisaged by the Government will diverge in many ways from the development lines we have followed in recent years. In the period 1969—74, employment in agriculture was annually reduced by 8 200 man-years, altogether almost 45 000 man-years. The number of farms was reduced by 6 800 per year, a total of 35 000 farms during the period, and the agricultural area which was farmed was reduced from 0.99 to 0.90 million hectares. The primary task is to alter the course of development so as to arrest the decline in the farmed agricultural area. In the main the increase in area must be effected in the period 1980—90.

The Budget Committee for Agriculture has worked out estimates of the manpower trends up to 1990. These estimates show an annual reduction of 3 300 man-years in the period 1974—80 and 900 man-years in the period 1980—90.

In considering these estimates, the Government sees little reason not to aim at a continuous rapid increase in efficiency in agriculture in the central areas, particularly with regard to production of plant products for the market. Programmes have also been prepared for a better utilization of other agricultural resources connected with the farms, particularly in forestry. This may contribute to a better utilization of manpower on the farms. Firmer regional policy measures may form the basis for a better utilization of manpower on many farms.

On the basis of an overall evaluation, the Government has come to the conclusion that the prerequisite increase in agricultural production in the period 1974—80 might be possible with an annual reduction in employment of an average 3 500 to 4 000 man-years. The employment estimates presented in Report No. 50 for 1974—75 to the Storting were based on a reduction of 27 000 man-years for the period 1974—80. Even if the new aim represents a lesser decline in agricultural employment, such is the degree of uncertainty attached to the employment estimates up to 1980, that this adjustment does not necessi-

tate the total revision of the figures in the above-mentioned Report.

The 1970 Population Census showed that 33 000 or 25 per cent of the 131 000 persons employed in agriculture were above 60 years of age. This age distribution will alone contribute to a considerable decrease in agricultural employment in the 1970's.

Production development and agricultural policy measures should be so shaped that the decline in employment and in the number of farms in the economically disadvantaged areas is considerably less than would be indicated by the average figures for the country as a whole.

The Government will closely follow developments in agricultural employment and production and will return to these questions in the Long-Term Programme for 1971—81.

An expansion of the agricultural area from 0.9 to 1.0 million hectares, and an increase in the cultivated area from 0.79 to 0.90 million hectares, will require that the reclamation of new land is kept at a comparatively high level. After making an overall evaluation, the Government has come to the conclusion that it will be sufficient over the next 10—15 years to reclaim about 8 000 hectares annually. The main part of this (about three-quarters) should be in the economically weaker areas. The land brought under cultivation in the central areas will largely consist of highly productive forest. Out of regard for future timber production, efforts will be made to limit the reclamation of such land.

The need for investment in agriculture is a question of central importance. In Report No. 50 for 1974—75 to the Storting on National Resources and Economic Development, it was calculated that the gross investment in agriculture will increase by 1.4 per cent per year in the period 1974—80. A considerably greater growth is now expected.

Calculations made by the Budgetary Committee for Agriculture show that the gross investments in agriculture will increase from 1 668 million N.kr. in 1975 to 1 887 million N.kr. in 1980, at 1974 prices (2.6 per cent increase per year). The increase from 1980 to 1990 is estimated to be about 0.5 per cent per year.

1.2.5 Coverage of Food Consumption

In Annex 6 (not translated) to this report, prepared by the Budgetary Committee for Agriculture, the development of the level of self-sufficiency (the Norwegian produced share

of the food consumed, on an energy basis) up to 1990 was calculated on the basis of the assumptions underlying the present report.

According to these calculations, the self-sufficiency level, which in the last few years has shown a slight tendency to fall, will increase from barely 48 per cent to 56 per cent in 1990. The increase in self-sufficiency will be a result of the increase in the production and consumption of agricultural products, from 40 per cent of the energy intake in 1973 to over 48 per cent in 1990. This increase is primarily based on an increased production of food grain and potatoes. The consumption of fish and fish products (including marine fat) will remain at a level of 7.5 per cent of energy consumption. This is because the increased consumption of fish will be balanced by the fall in the use of marine fat in the margarine industry. However, because of the expected increase in population, the consumption of marine fat on the Norwegian market in 1990 will equal 1973 consumption levels.

It is estimated that the degree of self-sufficiency (corrected for feed concentrate imports) will increase from 39 per cent in 1973 to 52 per cent in 1990.

The Budgetary Committee for Agriculture has calculated that the export of food and fodder corresponded to 13.5 per cent of the Norwegian population's energy consumption in 1973. These calculations do not include the export of marine oils. If the total export volume was used directly for human consumption, it would equal 25 per cent of the energy consumption of the Norwegian population.

In the Report of Norway's Resource Situation in a Global Context (NOU 1974:55), it has been calculated that the degree of self-sufficiency (corrected for feed concentrate imports) may reach 55 per cent. On the basis of the assumptions underlying the Government's nutrition and food policy, it will be possible to approach this level by 1990.

According to the estimates, Norwegian imports of food in 1990 will be mainly sugar (99%), food grain (72%), fat for margarine (40%) and other fats (80%), fruits and berries (65%), vegetables (15%) and fish (15%).

On the basis of the plan outlined in this report, Norwegian food security will be strengthened much more than is indicated by the increase in the nominal level of self-sufficiency. This is related to the fact that, according to the present assumptions our imports of feed concentrate will be very much reduced. The possibility of adjusting production and consumption in a crisis situation will thus be considerably increased.

1.3 NUTRITION AND FOOD POLICY MEASURES

1.3.1 Consideration of the Principle Factors Involved

An absolutely central question is that of the measures to be taken to influence the production and consumption of food products in accordance with the aims of the nutrition and food policy. The measures must be put into effect by collaboration between

- the public sector
- the organizations, enterprises and employees in the relevant economic sector
- the voluntary organizations
- the various categories of households.

The Government believes that the goals should be realized in close cooperation with the organizations, enterprises and people who are and will be involved in the work on this policy.

A country's diet is the consequence of a series of factors which are discussed in the Report. A comparison of the aims of the nutrition and food policy with the development tendencies found in Norway today shows that a number of these development tendencies must be altered if the aims are to be achieved within a period of 10–15 years.

Although nutrition and food policy ranges widely, the effect on each field will be relatively limited. What is decisive for the implementation of a national nutrition and food policy will be the degree of stability and the extent of coordination in its execution.

Measures may be divided into

- agricultural and fisheries policy measures
- price policy and consumer subsidies
- measures in respect of industrial processing and imports
- measures in respect of marketing
- information and education
- provisions as to content and composition of food products
- research

Our nutrition and food policy must to a large extent be based on the utilization of Norwegian production resources. A change in the pattern of the consumption of food products may lead to some transitional problems for enterprises and certain categories of employees. The Government will devote special attention to such problems.

1.3.2 Agricultural, Fishery, and Price Policies

In the Government's view, the planning of consumer subsidies and of measures of agricultural and fishery policy should be viewed together, because inter alia they can supplement one another within certain limits.

1.3.2.1 *Agricultural Measures*

Measures of agricultural policy are largely shaped within the framework of the Agricultural Agreement (between State and farm organizations). For several important agricultural products, the Norwegian market is protected in various ways against competitive imports from abroad. Within this framework prices are determined for the products, and various special economic measures to support production are introduced. In the Government's view, measures of agricultural policy should be shaped in such a way that they also serve considerations based on nutrition and health grounds.

The content of nutrients contained in agricultural products may be influenced, within certain limits, by plant breeding, and animal feeding and breeding measures. The most important measures are those aimed at changing the relationship between fat and other nutrients contained in livestock products. The problems in this respect are difficult and long-term, but the steps already taken in this field provide a good basis for further endeavours. The Government wishes to cooperate with the organizations in the milk and meat sectors on measures in these fields.

1.3.2.2. *Fisheries Policy Measures*

The price of fish and fish products is largely influenced by world market prices, since 85–90 per cent of the production is exported. This means that the fisheries policy measures which are introduced through the Fisheries Agreement will be able to influence domestic price levels only to a slight extent.

The establishment of a scheme of consumer subsidies compensating for value-added-tax in respect of fish, herring and whale meat has created some problems in connection with the marketing system for fish.

The Government's aim is to arrange as soon as possible for a thorough review of the domestic marketing of fish in order to ensure a rational and regulated market situation in which the control of margins and prices operates satisfactorily. Apart from the fact that this will probably contribute to an increase in fish consumption, the authorities will be better placed to introduce various policy measures.

1.3.2.3 *Price Determination*

The trading commitments undertaken by Norway will affect the opportunities for determining food prices more or less independent of the prices on the world market.

Due to differences in the protection schemes for the various products, the prices

of some food products are determined especially for the Norwegian market, while the prices of other goods are to a greater or lesser extent affected by world market prices. The foods, which are affected by the world market price of the product or of the raw material, include sugar, margarine, vegetable oil and fat, fish and fish products, as well as some of the vegetables, fruits and berries. Food grain occupies an intermediate position owing to the special price and subsidy schemes for food flour. Even for products for which there is an opportunity to establish a national price level, in many cases the practical possibilities will be limited. A greater degree of stability in the world market prices for food will facilitate the planning and implementation of measures in a nutrition and food policy directed towards a particular goal. In this connection it is significant that Norway has extended her support to the proposal for international commodity agreements. The work with such arrangements is now in progress, inter alia, in UNCTAD and GATT.

1.3.2.4 *Use of Consumer Subsidies and Compensation for Value-added-tax*

In the case of most products which are subsidized, the amounts of the subsidies are composed of compensation for value-added-tax plus direct consumer subsidies.

Consumer subsidies and compensation for value-added-tax are vital elements in the general economic policy.

It is important that the measures be applied to such products as may be reasonably certain to benefit the consumer and where the scheme may be put into effect with an uncomplicated administration and system of control. This restricts the number of products which it is technically possible to cover by the schemes. Today subsidies and compensation for value-added-tax have been introduced for liquid milk, cheese, most types of meat, butter, margarine, fish, Norwegian caught herring and whale meat, as well as for food flour. Furthermore, it is intended to allocate the subsidies and the compensation for value-added-tax in such a way that these instruments will particularly benefit families with children and consumers with low incomes. Moreover, it has been an important aim to see that these measures may be used as a flexible policy instrument in the short-term economic policy where, over a short period, there may be a question of both increasing and reducing the amounts.

In the Government's view, considerations of price policy must still represent an important base for its policy on subsidies.

The demand for products such as milk, cereals and potatoes varies only slightly with variations in price, while there is a tendency for the demand for cereals and potatoes to decline rather than to increase with increased income.

Meat, including pork, is an example of a product for which neither price fluctuations nor income play any great part in influencing demand. Just as important as regards these products are their prices in relation to one another — for example between meat and pork, and presumably the price relationship between meat and fish.

In deciding on consumer subsidies, in the Government's opinion it is important to aim at influencing the consumption of food in the desired direction with regard to nutrition and health. The Government is of the opinion that it will be possible to combine this goal with the goals of the policy on prices in respect of the use of subsidies.

Some consideration on points of principle has been given to the measures related to prices for the various products:

Food grain (food flour) should be relatively cheap and stable in price. Today we have a price system with a fixed food grain price independent of variations in the world market price.

With the present marketing system for potatoes, there has so far been no question of using subsidies. Possible consumer subsidies, and a system of measures as part of the agricultural policy, making the producers' incomes to some extent independent of prices, should be assessed, in relation to each other.

With the present marketing system for vegetables, fruits and berries, there is no question of using subsidies. To keep prices at a moderate level, in order to stimulate the consumption of vegetables, a system of measures in respect of Norwegian vegetables should be used so that the price from the producer is, relatively speaking, reduced through packaging grants, quality grants, production area grants and in other ways.

The prices of these products vary greatly geographically. The present freight grant schemes should be retained and consideration should be given to extending their scope with a view to ensuring cheaper goods in the areas at a distance from markets.

As for sugar, future international commodity agreements which Norway supports at the international level will contribute to keeping consumption at reasonable levels.

The price of margarine and butter should be determined jointly so that a reduc-

tion in consumption may be encouraged. The current subsidies on butter and margarine should be reduced and, if possible, removed.

The meat subsidies should be so arranged that, also in relation to fish, the per capita meat consumption is not increased. As an element in efforts to increase the degree of self-sufficiency, the meat subsidies should still be such that the consumption of «dark» meat (beef and mutton) is stimulated.

The determination of prices through the Agricultural Agreement (between State and farm organizations) and the subsidies for whole milk and lowfat milk should be considered together and so arranged that the consumption of low-fat milk is stimulated in comparison to whole milk.

It is fully justifiable as part of the nutrition and food policy both to increase and reduce the subsidy rates for these products. Low-fat milk should be introduced to provide the consumer with a better and more varied choice of liquid milk.

The determination of price, by means of the Agricultural Agreement, in respect of cream should be effected in such a way as to avoid stimulating consumption.

1.3.3 Industrial Processing

The food industry will play an important role, for example when it comes to providing the population with a differentiated, varied and appropriate selection of food products in accordance with the goals of the nutrition and food policy.

In this connection the Government will endeavour to establish close cooperation with the organizations of the food industry.

1.3.4 Distribution and Marketing

There are relatively large imbalances in the present marketing of food products, viewed from the angle of nutrition and health. In the long term, the goal ought to be that the distribution policy be so planned that the consumer is assured of a more appropriate selection of food products, presented in an acceptable way.

The current situation in regard to marketing and distribution may be due to lack of knowledge. Endeavours will be made to improve this state of affairs through close cooperation with the industries concerned. The possibility of making use of statutorily authorized measures should be kept open. It would be an unsatisfactory state of affairs if only Norwegian firms observed any relevant agreements.

The application of the Marketing Control Act is particularly related to incorrect and

misleading advertising. In the Norwegian Official Report NOU 1974: 61 «Advertising» it is proposed that a statute should be adopted to introduce an information requirement ensuring that consumers receive better information in regard to goods and services. On the basis of this report and the comments to it, the Government will decide on its attitude to the proposal.

The Government has proposed investment grants and operating grants to general stores in outlying areas. One of the conditions on which it is proposed to base the scheme is that the shop carries a selection of goods conforming to the goals of the nutrition and food policy.

The health regulations for marketing should be seen in a larger context than previously so that they may contribute to ensuring the availability of a good selection of suitable food products.

1.3.5 Large Households

Selective measures in respect of large households are both desirable and necessary.

On the basis of the report on the education of personnel in large households (NOU 1975: 36) and authoritative comments on the subject, the Government will take the necessary steps to ensure that the education in this field is satisfactory.

These large households represent a very large recipient of industrially manufactured food products. Effective cooperation between these households may be important for the shaping of products offered both to the large households as well as for general consumption.

Since the public authorities own and operate a large number of these households, the Government will help to see that cooperation becomes a fact and on the necessary scale. Cooperation with the National Nutrition Council is important, primarily in regard to the content of the teaching, which is to be provided.

1.3.6 Legislation

Current regulations in this field aim at, inter alia:

- preventing the manufacture and sale of foods dangerous to health,
- ensuring cleanliness and hygienic conditions,
- stipulating how products shall be manufactured, their contents, and the requirements they must satisfy before they can be offered for sale,
- preventing incorrect conceptions as to the origin, condition, nature, quantity, or composition of products, or other circumstances which are of importance to public

health, or for the consumer's assessment of the quality of the commodity.

The Government believes that laws and regulations can be useful and important means for carrying out the objectives of the nutrition and food policy.

Today a number of ministries administer various regulations, which may be of significance for nutrition and food policy. The interministerial body, which this report proposes be established, will be given the task of seeing that the best possible coordination takes place in this area, and also of assessing the necessity for improving and simplifying the regulations.

1.3.7 Research and Study

In several fields, research will provide new and wider knowledge which will have to be taken into account in nutrition and food policy in future. In this Report, the Government has only considered research and study of significance for the implementation of the policy. In several areas there is a need for research to be carried out as a necessary part of the implementation of nutrition and food policy measures.

In the Government's view it is natural that the proposed agency for research related to social planning should bear responsibility for the research work connected with implementation of the future nutrition and food policy. Research in this connection is being carried on today in several institutes and research councils. An important task for the new body will therefore be to coordinate research activities and to develop a useful form of cooperation with other research councils and the various research centres.

1.3.8 Education and Training

One of the important tasks involved in implementing a nutrition and food policy is for the schools to give the pupils insight into food production processes, both in theory and practice, and thus to lessen the gap between practical production life and the education situation.

Cooperation has been established between the Ministry of Church and Education, the Norwegian School Gardening Association and representatives for the counties of Hedmark and Oppland, for the purpose of working out a programme for contact between the schools and agriculture. The State gives grants for experiment with such contact in these counties. The results and experience gained will be made available to other counties.

Within the field of adult education and information there is a corresponding question

of principle, namely how the individual may organize his own existence in relation to nutrition and health. The Government regards adult education, the stimulation of small-scale gardening, allotment cultivation, etc., as important elements in the implementation of the nutrition and food policy.

1.3.8.1 *The Teaching of Nutrition in Schools*

Our dietary habits are formed at a very early stage of our lives. It is therefore extremely important that the teaching of nutrition should begin when children are still small and be followed up over the years. There are several unsolved problems on which further work must be done to ensure the best possible teaching on the subject of nutrition.

It appears to be necessary to ensure that training in nutrition is provided to pre-school teachers and other staff at kindergardens and day nurseries. In the case of pre-school teachers, this can be accomplished by giving higher priority to nutrition in the curriculum of the 3-year educational course for pre-school teachers.

The training of teachers in the elementary, junior and junior high schools must be strengthened — not only with regard to the subject of home economics, but also by the inclusion on a permanent basis of subjects covering nutrition in the natural science and parts of the social science curricula.

In further education — especially with regard to the vocational schools (schools for home economics and catering) — measures for keeping the teachers up-to-date are a prime necessity. Provision must therefore be made for further training and post-training courses for these teachers. The Council for Further Education and the Teachers' Training Council will take up the question of developing expertise from within their ranks to run post-educational and further education courses.

Experience and practical knowledge in the individual homes are of great importance in the development of food habits. It is considered important that practical training in the elementary school should run parallel to theoretical education and be strengthened in the years to come.

With regard to institutions for further education, teaching at the schools for home economics and the home economics divisions of the vocational schools for handicraft and industries is particularly important. These schools train 4,500 students each year. The aim of this education should be to contribute

to the following-up of the nutrition and food policy in the individual homes.

The situation with regard to teaching aids cannot be described as satisfactory. This is due to circumstances which affect the entire teaching aids field and which are at present being studied by a publicly appointed committee on teaching aids.

Up to now the Ministry of Church and Education has only financed the production of text-books for career education. An extension of this support is now under consideration.

1.3.8.2 *Teaching of Health Personnel*

Teaching on the subject of nutrition is included in the training of the various types of health personnel. It is very important that all types of health personnel should include health information as part of their work. Information as to correct dietary habits plays an important role here and instruction in the teaching of nutrition and proper diet should in future be given more emphasis in the study programmes. It will also be important for the subjects of proper diet and nutrition to be given higher priority in the further education and post-educational courses for medical personnel of all types.

1.3.9 *Information Activities*

The aim of information activities is threefold:

- it shall contribute to *motivation* for better dietary habits
- it shall contribute to securing broad general knowledge of the main principles of a proper diet
- it shall provide the possibility of acquiring the necessary skills.

The work of public institutions and organizations will form an important foundation for information activities.

A vital prerequisite if the information activities are to be effective and sufficiently co-ordinated, is that increased and improved information services should be coordinated with the preparation of good teaching aids appropriate to the pursue.

The National Nutrition Council should be responsible for ensuring that information work carried out as an element of the nutrition and food policy is balanced and properly substantiated.

In the general task of disseminating knowledge to the public, the work of the Consumer Council will be of prime importance. The Council has developed a nation-wide network at the local level which ought to be made responsible for further tasks in the years ahead.

To strengthen contacts between people whose

work concerns matters connected with nutrition, the Government will organize regular conferences on nutrition.

The National Association for Nutrition and Health occupies a special position among the voluntary organizations. The Association should continue its work in guidance, advice and information on nutrition and proper diet.

Information work should continue to build on the existing broad objective interest in nutrition questions in humanitarian and other voluntary organizations and among information agencies in Norway. In the opinion of the Government, the way should be prepared so that an important part of the information work may be carried out by organizations of this type and that special information material on the subject should be prepared for this purpose. The Government believes that public grants should be allocated for such activities and believes that 1 million N. kr. annually ought to be made available for the purpose. The National Nutrition Council should be responsible for ensuring that these activities are properly based. All sections of the population should be able to make use of this information, but emphasis should be put on information services being provided for the groups most in need of them. The motivation and the necessary knowledge to enable people to change over to better dietary habits are lacking. One important task for the information services is to ensure that the individual acquires the necessary skills.

1.4 INSTITUTIONS FOR THE FOLLOW-UP OF NUTRITION AND FOOD POLICY

If the nutrition goals are to be attained, an absolutely decisive factor will be the establishment of close cooperation between industrial and trade organizations, economic enterprises, various categories of household, voluntary organizations and research institutions.

This being so, the authorities must develop institutions which can be responsible in future for the coordination and further development of the nutrition and food policy.

The implementation of the policy will require that specific institutions are responsible for:

- describing and analysing developments in dietary habits and nutrition in the short and long term, based on the nutrition goals
- defining projects and develop plans for both the long-term and the annual implementation of the nutrition and food policy
- to propose measures

- ensuring that the necessary measures are carried out within specific time limits
- coordinating the work done by the different ministries and ensuring that due regard is paid to nutrition and food considerations in the various fields
- assessing the effectiveness of the work carried out
- contributing to a satisfactory professional development in the field of nutrition
- ensuring cooperation with trade and voluntary organizations
- advising the governmental and other public authorities.

The implementation of a policy on nutrition and food must be based on a long-term adaptation of measures which are being presently followed. The responsibility for these measures is in the main divided between the Ministry of Fisheries, the Ministry of Consumer Affairs and Government Administration, the Ministry of Environment, the Ministry of Trade and Commerce, the Ministry of Church and Education, the Ministry of Agriculture, The Ministry of Social Affairs and the Ministry of Foreign Affairs.

To ensure satisfactory cooperation in the planning and implementation of the nutrition and food policy, and to ensure that this cooperation is properly based, the Government will advocate the following administrative solution:

1. Establishment of an interministerial coordinating body.
2. Reorganization of the National Nutrition Council.
3. Establishment of an office for nutrition in the Ministry of Social Affairs.

1.4.1 Coordinating Body for the Ministries

The Government believes that it will be necessary to establish a coordinating body for the work carried out by the various ministries in connection with the nutrition and food policy.

This body shall, inter alia, define projects and draw up plans for both the long-term and the annual implementation of the nutrition and food policy. It is not intended that this body should be responsible for coordination related to food supply policy.

The ministries concerned shall be represented in the coordinating body by one or several senior administrative officers from the relevant fields. The Storting shall be kept informed in the annual programme of work and budget proposals from the Ministry responsible for the coordination of the nutrition and food policy and from the other ministries involved.

1.4.2 National Nutrition Council

The Government will still need an institution able to provide specialist advice on questions of nutrition. In many matters in this field an all-round competence not possessed by any one person or any specialist group is needed.

With this in mind, it is possible to outline the following tasks for the National Nutrition Council:

1. To be an advisory body for the central Government administration and other public authorities in matters concerning nutrition.
2. To give expert advice and opinions to others, for example voluntary organizations, large households and the food industry.
3. To be responsible for describing and analysing the short-term and long-term dietary situation in Norway.
4. To submit proposals for new measures.
5. To make recommendations, on the basis of specialist knowledge, concerning the allocation of funds to information activities.
6. To contribute to a satisfactory development in the field of nutrition.
7. To assess the effectiveness of nutrition activities in Norway.

The National Nutrition Council should be composed of qualified personnel from the various branches engaged in nutrition, consumer and supply questions. The individual ministries ought not to be directly represented in the Council.

The National Nutrition Council should have the economic means to enable it to allocate projects to other institutions as part of the work of developing expertise in the field of nutrition.

It is assumed that in future the National Nutrition Council should be mainly concerned with national nutrition and food supply questions.

It is assumed that the international liaison functions which have hitherto been handled by the secretariate of the National Nutrition Council could be dealt with by the ministries concerned, i.e. primarily the Ministries of Agriculture, Fisheries and Foreign Affairs.

The National Nutrition Council should, as now, be administratively associated with the Ministry of Social Affairs.

1.4.3 Administrative Follow-up

After reviewing the question in all its aspects, the Government has reached the conclusion that the coordinating responsibility for nutrition and food policy should continue to lie with the Ministry of Social Affairs.

Considering the increased emphasis the Government attaches to nutrition and food policy, as is also expressed in the proposal for an interministerial coordinating body, the Government will propose the establishment of a separate office for nutrition questions (Nutrition Division) in the Ministry of Social Affairs.

The Nutrition Division will be responsible for the administrative handling of nutrition questions. This implies that the division must, *inter alia*, act as secretariate for the interministerial coordinating body and for the National Nutrition Council and its sub-committees.

The Government will return to this matter when the Storting has debated the present report.

Chapter 2. Nutrition and Health

2.1 HISTORY OF NUTRITION POLICY

In this section the history of nutrition policy will be dealt with briefly, as well as national and international measures which have been adopted with the aim of implementing a nutrition policy.

In their book «The Diet in Norwegian Homes with small Incomes: Reality and Future Goals», which was published in 1937, Karl Evang and Otto Galtung Hansen wrote:

«The time is long past when the solution of the dietary problems of the population could be principally entrusted to the varying degree of knowledge of individual housewives and to random private business initiative. The nutrition question has become a social problem, which can only be satisfactorily solved in modern cultural states through social organization.» (op.cit. p. 168)

The history of nutrition policy reveals how the acknowledgement of these ideas has gradually gained ground.

The nutrition policy which has been followed at each point in time has been related to the development of the science of nutrition, diet research, the supply of food and the increasing industrial processing of foodstuffs, as well as to the living standards of the population.

Experience in food and nutrition has been handed down from generation to generation. But the modern science of nutrition was first established at the beginning of this century. At the same time scientific and technical advances provided the basis for the modern food industry. The progress in nutritional research at the beginning of this century occurred at a point in time when there was widespread poverty and need in many countries in Europe and America. Many poor people existed on an inadequate and unbalanced diet. Children and young people were retarded in growth and physical development, and deficiency diseases such as rickets were not uncommonly seen also in our country. To a lesser degree this was true also for scurvy and night blindness.

To counteract this the Norwegian social welfare service undertook such programs as direct distribution of food. Valuable dietary work was also carried out through the health stations.

In 1933 the Food Act was passed.

In 1936 the Oslo City Council appointed a committee «to carry out an investigation of the nutritional situation of persons receiving public assistance». The Committee's recommendations regarding the diet of children,

adults, and pregnant and breast feeding women were presented in 1937. That same year a National Nutrition Council was established.

The nutritional problems in the western industrialized countries were such a cause for concern in the 1930's that they were discussed in detail at the League of Nations. The League proposed that each individual country should assume the responsibility for a nutrition policy of its own, which should be implemented to promote public health and encourage agriculture.

The guidelines for a concrete policy drawn up by the League of Nations without doubt played an important role in the planning of food supplies in many warring and occupied countries during the second world war.

During the war the groundwork was laid for The Food and Agriculture Organization of the United Nations (FAO), which was established in 1945.

In accordance with the recommendations for member countries, the Norwegian government established the National Nutrition Council in 1946.

The National Association for Nutrition and Health was founded in 1955 in cooperation with the Directorate of Health and the National Nutrition Council.

In 1962 FAO and the World Health Organization together established the Codex Alimentarius Commission, which was given the task of elaborating international standards for foodstuffs.

The Norwegian government decided to establish a National Codex Alimentarius Committee in 1970. The World Food Conference in 1974 was another step towards promoting an international interest in nutrition policy.

Today it is more important than ever that a knowledge of nutritional requirements and diet forms the basis for planning the production and distribution of food in individual countries and in the world community.

Through investigations carried out by the World Health Organization and FAO it has been established that considerable segments of the world's population suffer from under- and malnutrition. It has also been acknowledged that the prevailing diet in the industrialized countries should not be a model for nutrition policies in the developing countries. Economic and industrial development has eliminated many of the nutritional problems which were widespread in Norway as recently as the period between the two world wars. At the same time this same development has

given rise to new nutritional problems which pose a serious challenge to Norwegian research, voluntary organizations and the authorities.

The nutrition policy which was evolved by the League of Nations in the 1930's was based on the economic and social conditions which prevailed in the western world at that time. Since the second world war it has become clear that poverty and need prevail in many developing countries, and it is to these which the principles of the United Nations nutrition policy apply most. In the rich industrialized countries we are now confronted with other nutritional problems which are related to an abundance of goods and abundant and diversified food supplies.

In 1972 FAO presented a definition of a food and nutrition policy. It was defined as being a complex of educational, economic, technical and legislative measures designed to reconcile projected food demand, forecast food supply and nutritional requirements.

The objective is to exploit production possibilities deemed feasible in relation to the national resources of the country and to hinder the development of consumption patterns likely to create health risks. A food and nutrition policy is therefore an integral part of preventive public health efforts. Practical planning requires coordination between the public authorities and many sectors of the economy.

2.2 NUTRITION AND DIET

Nutrition and diet are two important factors in our environment and way of life which influence health. Through food and drink the organism is supplied with substances which are necessary for growth and maintaining health, and the need for energy is satisfied. The science of nutrition is primarily concerned with clarifying the amounts of ingredients in the diet which are necessary for obtaining satisfactory growth and development for all groups in the population throughout their lifespan.

Pregnant and breast feeding women, infants, children and youths, adults and the elderly have different nutritional needs which are determined by their physiological conditions. A diet which contains inadequate amounts of nutrients or nutrients in unbalanced amounts can lead to illness or contribute to the occurrence or development of diseases. Therefore a sound diet plays an important role in preventive health work and is an important factor in the treatment of many diseases.

In the course of the past 100 to 150 years

nutrition research has developed into a well established branch of science.

Basic studies on energy were begun towards the end of the last century, and the energy requirements for all age groups, various occupations and under various forms of physical activity have since been largely established. During the first half of this century vitamins were discovered, their chemical composition clarified and occurrence in foods mapped, their importance for metabolism better understood and the approximate quantitative human requirements determined. In the past 25 years a great deal of work has been done, and it is now possible to assess the nutrition quality of the diet on the basis of its qualitative composition with regard to a number of essential nutrients (such as proteins, essential amino acids and fatty acids, vitamins and a number of minerals), and to relate this with the requirements in various physiological situations.

It should be noted that continuing efforts are being made to determine the precise quantitative requirements for a number of nutrients.

Moreover, the discovery of other vital and/or desirable dietary factors cannot be ruled out.

The health condition of a population can be defined on the basis of a number of factors. Lifespan, body height, mortality rate, illnesses such as tuberculosis and other infectious diseases are health criteria for which there are comparatively good statistics covering many years. It is difficult to trace the development over time of other diseases and indications of reduced health such as dietary deficiency diseases, tooth decay, iron deficiency anemia, obesity, etc. because satisfactory studies are lacking.

2.3 UNDERNUTRITION AND DEFICIENCY DISEASES

The close relationship between nutrition and physical and mental well-being has been well known throughout human history. In times of food scarcity, this relationship shows itself in hunger and reduction of body weight, reduced working capability, increased susceptibility to infectious diseases and increased death rate.

In a world context undernutrition continues to be one of the most important causes of sickness and death. In many developing countries an insufficient supply of energy and proteins is the most important of all nutrition problems and hits infants and small children hardest of all.

An insufficient food supply in itself results

in a scant provision of the essential nutrients. If in addition the available diet is unbalanced, the risk of more specific dietary deficiency diseases, including vitamin deficiency diseases, increases.

In many poor developing countries the average lifespan is still short. There is a high death rate, especially in the first years of life. The high rate of disease and death in the early years of childhood is especially due to inadequate consumption of energy and proteins. It is also due to lack of essential nutrients. Resistance to infectious diseases is reduced. Undernutrition retards growth, hinders development and weakens working capability. Poor health arises not only as a result of improper nutrition, but also because of unsatisfactory environmental and hygienic conditions, inadequate health services, lack of education, etc.

Undernutrition and dietary deficiency diseases hit hardest those groups in the population which are worst off, both among rural populations and people in urban slum areas. A privileged minority in the developing countries, which has access to an ample diet, does not have health problems of this type.

In our country an insufficient diet has also been the cause of a good deal of disease and death, especially during wars, blockade, crop failures or economic crises scarce supplies of certain essential nutrients have probably been usual at certain periods in our history.

However, in the course of the past 25 years undernutrition and dietary deficiency diseases have been practically eliminated in Norway.

2.4 OTHER FORMS OF MALNUTRITION

The average lifespan in the industrialized countries is high today because, for one thing, illness and death in early childhood have over a period been greatly reduced. However, health problems have arisen instead, which are related to over-consumption and unbalanced amounts of nutrients in the diet. Among these we should note cardiovascular diseases (including heart infarct), tooth decay, obesity and certain forms of digestive and metabolic diseases. Some of these forms of malnutrition were largely unknown before the second world war, and are comparatively rare in countries with low standards of living and simple diets. By far the greatest cause for anxiety lies in the increase in the cardiovascular diseases, because of the considerable incidence of death, sickness and disability these cause.

The cardiovascular diseases comprise a

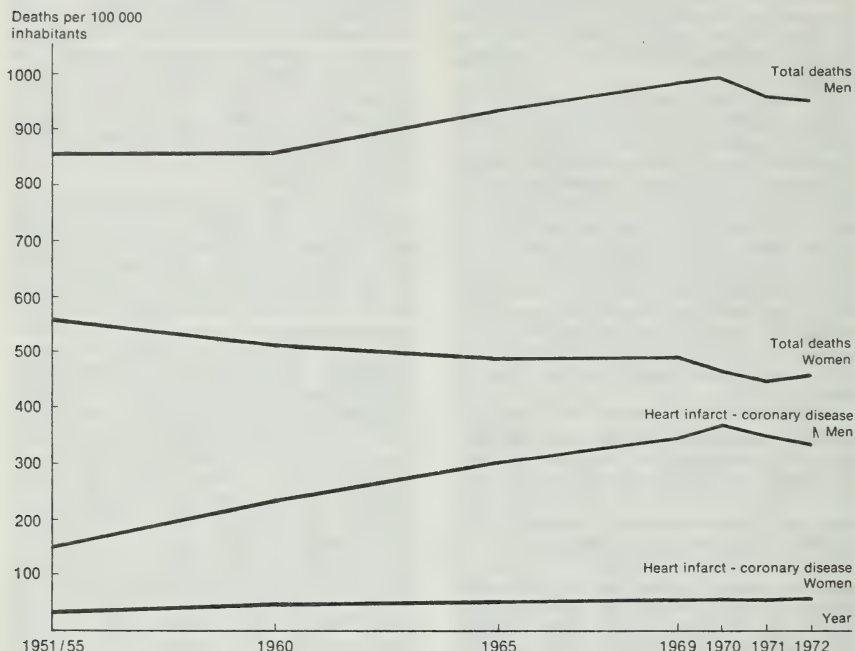
number of individual diseases, but it is the atherosclerotic cardiovascular diseases which are especially dominant and which have shown an alarming increase since the last world war. Somewhat simply stated, the basic disease can be related to the changes which take place in the human arteries with advancing age. The degree of atherosclerotic change is *inter alia* related to the amount of cholesterol in the blood.

The cholesterol level in the blood is affected by many circumstances, including heredity, age, hormones and composition of the diet. As far as the composition of the diet is concerned, we know especially that the amount and quality of fat plays an essential role. A more detailed explanation can be found in Appendix 1. The causes of the atherosclerotic cardiovascular diseases are not fully understood. Comparative studies of population groups in different parts of the world have revealed a relationship between a high intake of saturated fats and an increased frequency of ischemic¹⁾ heart disease. People who traditionally exist on a diet which has a low fat content and relatively high amount of polyunsaturated fats show a lower frequency of heart attacks. Studies show that atherosclerotic changes develop at an earlier age and to a more marked degree among people in affluent societies than among those in developing countries. The average level of cholesterol and other types of lipids in the blood is also higher in the populations of affluent societies than in countries which have a lower standard of living. However, such data must be carefully interpreted. The various population groups differ from each other in many ways, such as in other dietary factors (for example, type and amount of carbohydrates), eating and meal-time habits, physical activity, smoking habits, hereditary characteristics and other factors. Still, it must be stressed that studies in industrialized countries have clearly indicated that increased amounts of cholesterol and certain other lipids in the blood are accompanied by an increased frequency of ischemic heart disease and other atherosclerotic diseases. In the past ten years cardiovascular diseases have reached alarming proportions in many parts of the industrialized world.

Over half of all deaths in Norway now occur as a result of cardiovascular diseases. The death rate from the individual groups of dis-

¹⁾ Ischemia means a local lack of blood. Ischemic heart disease applies to the two illnesses which result from a poor supply of blood to the heart muscle itself, i.e. heart infarct and angina pectoris.

Figure 1 Development in the total death rate and death rate from heart infarct, coronary disease for men and women in the age group 50-59



eases within the cardiovascular disease complex varies according to age and sex.

Ischemic heart disease, which is the largest group, has showed the greatest increase, being most pronounced in men.

The largest increase has been among men under 70 years of age, and especially in the age group from 40 to 50 years. In the period 1966-67 the death rate from heart attacks and coronary disease in the 40-49 age group increased 280% for men and 190% for women as compared with the period 1951-55.

However, the rate of increase has fallen somewhat during the last few years.

Figure 1 shows the total death rate and the deaths from heart infarct, coronary disease for men and women in the 50-59 age group.

Tooth decay is a very widespread disease in many industrialized societies. Norway is among those countries in the world which have the highest incidence of this disease.

Not only does tooth decay affect nearly all Norwegians in childhood. An equally serious social problem is the fact that tooth decay occurs repeatedly throughout life, or as long as we have our own teeth.

Investment of time and money both public

and private in an individual set of teeth is thus considerable when seen in the perspective of a lifetime.

The wide occurrence of tooth decay is related to the high consumption of foods with a high sugar content and the frequent intake of soft drinks, chocolate and candies etc. containing sugar.

Sugar is by far the most significant of factors which cause tooth decay. Susceptibility to tooth decay is sharply reduced when fluorine is absorbed into the tooth enamel.

In recent years the Ministry for Social Affairs has granted subsidies for a systematic distribution in several countries of fluoride tablets to children and preliminary reports indicate a marked reduction in the frequency of tooth decay. In addition attention is drawn to the information on the use of fluorides in the prevention of tooth decay in Government Report No. 111 (1973-74) to the Storting and in parliamentary committee report S. No. 138 (1974-75).

Obesity is prevalent among persons of middle age and it seems also to be a growing problem among children. The most common cause of obesity is increased deposits of fat

in the body, resulting from a greater supply than consumption of energy. From a health point of view obesity is important because it is accompanied by increased illness and death as a result of high blood pressure, cardiovascular disease, diabetes and gallstones. Because of overloading, obesity can also lead to diseases of the joints and skeleton.

Some diseases of the stomach and intestinal tract are believed to be affected by diet and nutrition. It is claimed that the modern diet, which is comparatively poor in plant fibres from bread and other cereal products, leads to a condition in the bowel which can be a contributory cause of constipation, hemorrhoids and other organic illnesses of the large intestine.

It is probable that dietary factors are involved in certain forms of malignant tumors (cancer) in the digestive tract.

Hemoglobin studies indicate that iron deficiency anemia is quite common in our population, especially in women between the ages of 15 and 50.

2.5 THE HEALTH AND NUTRITION SITUATION IN NORWAY DURING THE LAST 75 YEARS

The health situation as measured by a number of criteria has improved considerably in our country since the turn of the century. Growth and development of children and youths have improved. One indication of this is increased body height.

Infant mortality has been greatly reduced. While the death rate in the first year of life per 1000 births was over 90 at the beginning of the century, it was 11.8 per 1000 in 1972.

The deathrate for children and youths has also dropped. Consequently life expectancy at birth has increased by about 20 years for both women and men during the past 75 years.

The life expectancy of men over 40—50 years, however, has not increased significantly. Indeed between 1950 and 1970 the number of years of life remaining for men 50 years old actually showed a decline.

The frequency of a number of diseases has been markedly reduced. There has especially been a decline in tuberculosis. This was one of the most important causes of death at the turn of the century, but it has gradually been reduced to the very low level of today.

While dietary deficiency diseases such as rickets and scurvy were seldom in the first ten years of this century, practically speaking they have disappeared since the last war.

The pattern of food consumption has changed considerably since 1900. On the basis of data on the total food supply (Table 1, Appendix 1) the consumption of food grains has decreased considerably, as has the consumption of potatoes. Eggs, fruits and berries, vegetables, edible fats and sugar have taken a considerably larger place in the diet, while the consumption of meat and fish and of milk has shown a more moderate increase.

These trends were clear and predominant up to the 1960's. Since then they have not been as distinct. For some of the food products concerned it appears that development is now on the point of taking another direction.

The diet has become more abundant and more balanced. The overwhelming majority of the population is quite well supplied with the essential nutrients such as proteins, minerals and vitamins. This does not preclude the fact that certain individual groups might have a somewhat scarce supply of certain nutrients such as iron.

There has been a shift in the amount and type of energy providing nutrients. The proportion of fats in the energy supply has increased, the increase mainly consisting of saturated fats. (A more detailed study is presented in Appendix 1.) The proportion of carbohydrates has declined, due especially to the reduced consumption of grains. The decline in the carbohydrate content of the diet has therefore been at the expense of starches, while the proportion of sugar has increased.

The total protein content in the diet is practically unchanged, but there has been a shift from plant to animal proteins.

During the second world war the food supply situation in Norway enforced dietary changes. The consumption of sugar fell to less than half, while the consumption of flour, grain, bread, potatoes and vegetables increased.

The flour had a higher milling degree (extraction rate) during this period, and there was a certain scarcity of food.

One result of these changes in food consumption was that the fat content in the diet dropped.

The spartan diet of the occupation years can be regarded as a huge experiment from the standpoint of health and nutrition. The frequency of tooth decay among pre-school and school children, for example, dropped considerably, and this improvement continued until 1946—49 when the situation again deteriorated. Similarly, the death rate from cardiovascular diseases (especially ischemic heart disease) dropped after the outbreak of war.

2.6 CONCLUSIONS

The general health situation today is undoubtedly better than it was 75 years ago. Cardiovascular diseases, however, have gradually become very prevalent in our country and now constitute one of the greatest threats to public health. Because of these and other diseases related to our current diet, it is necessary to have a more defined nutrition and food policy.

The survey of diseases conditioned by nutrition which is presented here is not complete. Without doubt future research will increase our knowledge of the relationship between nutrition and health. However, we already know enough about nutrition and health to be able to make clear recommendations to the general public.

The primary objective of our nutrition policy must be to procure adequate, safe and suitable nutrition for the population.

Norway should have a supply of food products which provides adequate energy and which assures a sufficient supply of all necessary nutrients and other desirable dietary ingredients. The diet which is offered must be safe in the sense that it provides the basis for good health and does not have harmful effects. In addition, the diet must be suitable to provide dietary habits of available food products, the supply situation, etc. given the necessary consideration.

One of the tasks of the National Nutrition Council is to make recommendations concerning the nutritional composition of the diet. Such recommendations were first made in 1954, and since then they have been revised every few years. Originally these only covered the supply of certain essential nutrients. In recent years advice has also been given on the optimal amounts of energy providing nutrients, especially fats, in the diet. The current recommendation on this point is briefly that the proportion of energy from fat should not exceed 35%. The ratio between polyunsaturated and saturated fats should be altered to increase the proportion of polyunsaturated fats. A reduction of the fat content in the diet requires a corresponding increase in the carbohydrate content. It is presupposed that the proportion of starches should increase, while the share of sugar in the energy supply should be limited.

An increase in the milling degree of grinding of bolted (sifted) wheat flour should be considered, which would result in greater

supplies of certain minerals, vitamins and plant fibre.

Practical considerations make it difficult to increase the fluorine content in the diet to any appreciable degree, and so this must be supplied by other means.

If these nutritional changes are consistently followed from an early age they will undoubtedly be very beneficial to health.

To improve the diet alone is not enough. Other conditions which increase the risk of sickness and are harmful to health must also be changed.

With regard to the cardiovascular diseases it is important to curtail tobacco smoking and promote physical activity, to avoid overweight and prevent and, if necessary, treat high blood pressure.

To achieve good results it is important to coordinate the nutrition policy with the overall health policy.

2.7 NUTRITION AND PREVENTIVE MEDICINE

The tasks of the public health service fall within the areas of preventive medicine, treatment, rehabilitation and care. The health service operates partly without and partly within institutions of various sorts and is carried out by personnel with training of varying types and degrees. The public health service is based to some extent on the need of the population for health services, but depends primarily on the available economic and personnel resources.

Modern medicine makes it possible to offer better opportunities for treatment to more people than previously. Great progress has also been made in preventive medicine, especially with regard to infectious diseases. This has resulted in an extension of the average lifespan, primarily because mortality in the youngest and younger age groups has been greatly reduced. This development now shows signs of levelling out, not least because of the increased incidence of cardiovascular diseases during the past 20–30 years, which especially hits adults and the elderly.

The development which has taken place, though somewhat differing from country to country, shows that living standards, including diet, have played an important role. There are many indications that a correct diet can help to turn development in favourable directions, and that it will continue to be an important factor in public health.

Chapter 3. The Global Nutrition and Food Supply Situation and International Cooperation for Solving Nutritional Problems

3.1 THE GLOBAL NUTRITION SITUATION

Hunger and famine have been a part of life throughout the ages. Until the beginning of the last century many people in our own and other European countries died from lack of food, when there were crop failures and bad years. Right up to the present time population groups in our own country have been mal- and undernourished.

In the course of the last hundred years new production techniques for agriculture and fisheries have been developed in our part of the world. These have radically increased our ability to utilize resources for food production. This has occurred together with and as a part of the growth of the industrialized society. The increased prosperity created by this development has enabled Norway and other countries with limited production resources to cover some of their food requirements through imports. The enormous production resources which were made available through the development of the North American continent secured the necessary grain supply for developing the food consumption pattern we now have, with a high consumption of domestic animal products.

Only a limited part of the world was involved in this process. In 1970 the industrialized countries had a population of 1,070 million people, or scarcely 30% of the total world population. These countries produced approximately 60% of the most important food products. They have a consumption of 3,000—3,200 calories per person per day, and of this domestic animal products supply 40—50%. A high consumption of foods of animal origin used to be considered a criterion of a well-balanced diet. Because of this high consumption of livestock products, the per capita grain consumption is very high — 400—500 kg in Europe and approximately 1000 kg in North America. Only 70—80 kg of this grain is used directly as food; the remainder is used indirectly in the form of fodder for domestic animals. Food production has increased faster than the growth in population, which has been moderate. It is estimated that the population in the industrialized countries will grow by about 20% from 1970 to 1990.

On the other hand we have the developing countries in Asia, Africa and Latin America with 2,550 million inhabitants in 1970, or 70% of the world population. It is estimated that their population will increase to more than 4,000 million by 1990. These countries produce

only 40% of the most important food products. They have a food consumption of about 2,200 calories per person per day. The vegetable foods — grains, including rice — predominate. It is cautiously estimated that 460 million persons in the world today are malnourished. It has been difficult to increase food production in the developing countries to keep pace with the growth in population.

This description of the food situation and the division of the world into industrialized and developing countries is very rough and conceals great variations within the two groups. There are groups in the developing countries which have satisfactory nutrition conditions, and there are groups of people in the industrialized countries, who do not have the economic means to provide an adequate diet.

3.2 INTERNATIONAL COOPERATION IN THE FOOD SECTOR

At the first world food conference, which was held in Hot Springs, Virginia, USA, in 1943, it was established that there has never been enough food produced in the world to provide everyone with a well balanced diet. It was also stated that poverty was the primary reason why many countries could not provide all of their population with sufficient food. Economic development is therefore a prerequisite for solving many nutrition problems. The marked population increase, which we have experienced in the post-war period, has resulted in a deterioration in the food situation despite a considerable growth in production. Surplus problems in the industrialized part of the world and the consequent large surplus stocks, especially in the USA, are not the result of actual overproduction. They are the result of an unsound distribution of goods.

3.2.1 Food and Agriculture Organization of the United Nations (FAO)

The Food and Agriculture Organization of the UN (FAO) grew out of the food conference in Hot Springs and was established in 1945. FAO is one of the specialized agencies of the UN and has 136 members (November 1975). Norway has participated in the work of FAO since its establishment and is at present observer in the Council of the organization.

FAO, which is an agency for international cooperation on questions of nutrition and

food supply, has the special task of reducing the poverty, malnutrition and hunger which today affect a large part of the world's population. It works mainly with studies of food supply problems of developing countries, on the basis of which FAO offers help in the form of advice and transfer of technical and financial assistance.

FAO's programme is especially aimed at implementing projects. The expenditures involved in projects financed by the UNDP¹⁾ in 1975 amounted to almost half of FAO extra budgetary resources. For the period 1975-80 it is estimated that FAO will be responsible for administering UNDP projects to a value of 700 to 800 million dollars. The total expenditure for UNDP project activity in this period is estimated at about 2 billion dollars.

In addition, indirect support is given by FAO to the developing countries to help them obtain economic assistance for undertaking various development measures within the fields of nutrition and agriculture. This support is in the form of pre-investment studies undertaken by the organization which may result in financial support on a bilateral basis. Often FAO also assumes the responsibility for carrying out bilateral programmes on behalf of the donor countries.

FAO is also a forum for international discussions, decisions and measures in the field of nutrition and food supply policy, food security, commodity problems, fishery agreements and protective measures for plants and domestic animals.

FAO's regular budget for the biennium 1974 and 1975 is about 105 million dollars; Norway's contribution in 1975 was about 2 million N. kr. In addition the Nordic countries finance approximately 25% of the UNDP activity, of which about one third is channelled through FAO.

3.2.2 The World Food Programme

The World Food Programme was established in 1963 by FAO and the UN. The programme is a multilateral body for food assistance and it mainly bases its assistance work on utilizing food surpluses of donor countries. The contributions of participating countries are made on a voluntary basis, and consist of food commodities, cash and services, of which about two thirds is food.

The main objective of the programme is to promote economic and social development. Some food is given directly to children as well as pregnant and breast feeding mothers in

order to improve their health. Some is made available to farmers involved in projects for agricultural development until these projects provide the necessary yield. Food is also contributed for development of the infrastructure in receiving countries, as payment for the workers who take part in the projects.

In addition to the more longterm development activity, the programme contributes food assistance in emergency situations. In 1975 55 million dollars of the Programme's budget are earmarked for use in emergency operations.

The Programme's budget target for the 1975-76 period is set at 440 million dollars, but because of a strong increase in the contributions by some donor countries it is expected that the total resources for the period will reach about 650 million dollars.

Norway has been a contributor to the World Food Programme since its establishment in 1963. Our food deliveries have mainly consisted of fish products. A regular Norwegian contribution of a value of 75 million N. kr. has been pledged for 1975-76. In addition considerable extra contributions have been made.

3.2.3 The World Food Conference

The question of assembling a World Food Conference was raised following the crisis in the global supply situation in 1972. That year there was the greatest drop in world food production since the second world war. As a result there was hunger and famine in many countries and large price increases on the world markets. The world stock of basic food commodities declined to a new low level and has not increased since. Rebuilding the stocks to a level which provides security against repeated food emergencies is scarcely possible without a considerable increase in production. This situation and the strongly increased dependency of the developing countries on food imports were the focal points in the preparatory work for the World Food Conference and during the Conference itself.

At the World Food Conference it was agreed that a solution of the world's food problems must take place within the framework of general development and international economic cooperation. The concrete problems of hunger and malnutrition, which were the original motivations for the Conference, were considered in connection with the general and many-sided problems facing the developing countries. Thus the Conference became one of the several conferences held after the sixth special session of the UN General Assembly, where the developing countries took the lead for the implementation of an action

¹⁾ United Nations Development Programme.

programme for a new international economic order.

The serious consequences of the global food problem and the increasing international interdependence fostered a strong desire to reach agreement.

The Conference adopted a declaration on the elimination of hunger and malnutrition and passed 22 resolutions relating to three main elements of a global food policy:

- 1) Increased food production in all countries.
- 2) Improved nutrition through a better distribution of food and improved consumption patterns.
- 3) Establishment of a system of global food security (Undertaking on World Food Security).

The Food Conference agreed that the most important element in such a global strategy for solving the food problem would be increased food production in the developing countries. This was regarded as the most important solution in the long run.

In the main resolution on objectives and measures for food production the question of increased food production in the developing countries is tied to such factors as internal structural conditions, level of investment and trade policy. The problems created by the scarcity and high prices of important input commodities, especially fertilizers, were also stressed.

The Food Conference answered these questions in a series of resolutions.

The developing countries must base themselves on a maximum utilization of resources through a policy which can mobilize the great masses of their population in active participation in the development process, especially in rural areas. In this connection, special emphasis was given to the important role of women and the situation of the poor small farmers and agricultural workers.

The question of measures for increasing food production in the developed countries was taken up for consideration during the conference itself. In the resolution which was adopted, the developed countries were requested to implement measures which would encourage a rapid expansion of food production. The importance of fish products in improving the quality of nutrition was noted. However, it was stressed that these guidelines must not slow down the increase in food production in the developing countries. This applies both to production for the domestic needs for these countries and for export.

The industrialized countries and the international organizations were requested to pro-

vide assistance in all these areas. The appeals to the industrialized countries, however, were closely tied to increased aid to agriculture and to trade policies, which the developing countries consider important both for general development and for increased food production.

The resolution on an international fund for agricultural development must be viewed in this connection, and several industrialized countries in this respect agreed with the proposal made by the majority of the oil producing countries (OPEC) and a number of other developing countries. Many of the developed countries also supported the establishment of the fund, but it remains to be seen whether adequate means can be obtained to bring it into operation.

Trade questions were given great attention during the Food Conference. A separate resolution was devoted to these questions because the developing countries wanted to debate the relationship between trade policy and food problems. Since the food crisis is a poverty problem, the developing countries emphasized that they are dependent on increasing their export revenues in order to intensify their development progress. In view of the fact that the developing countries are primarily producers of food commodities and tropical raw materials, they felt that the industrialized countries must on the one hand take measures to increase access to their markets and on the other support measures to stabilize trade with these products. Some developing countries are exporters of food commodities while others are net importers. The fact that the developing countries nevertheless succeeded in maintaining a unified external front is due to the strong group solidarity which they have mobilised at international conferences in recent years.

The Norwegian delegation supported the request of the developing countries to debate food problems in connection with trade policy. There was a positive reaction to measures which would stabilize and stimulate the prices of such products primarily exported by these countries. Norway also approved the demand for an increased liberalization of imports from the developing countries. However, it was pointed out that it would scarcely be in the total interest of the developing countries to have increased access to markets result in a one-sided flow of food products from the developing to the industrialized countries. A long-term objective should therefore be to develop new international arrangements which would increase regional trade in food products between the developing countries.

The resolution on trade question which was unanimously adopted was a compromise: The extensive demands of the developing countries for a one-sided liberalization of trade were not met, but the resolution strongly requested the industrialized countries as much as possible to have in mind the export earnings of the developing countries when formulating domestic support measures for agriculture.

The Food Conference passed an extensive resolution on the other basic element in this global strategy, i.e. better nutrition through improved patterns of consumption and distribution of food, with guidelines and programmes for improved nutrition. The central point in this resolution is that better utilization and distribution of the world food resources are necessary to assure that increased food production reduces hunger and malnutrition. Therefore all countries were urged to introduce intersectorial nutrition planning.

In this respect the Food Conference also stressed that malnutrition is closely related to poverty and an unequal distribution of income both between and within the individual countries. The pattern of consumption and the over-consumption in the rich countries was criticized both for its harmful effects on health and from a distribution point of view. The Food Conference especially criticized the use in industrialized countries of large amounts of grain as feed in order to cover the high consumption of animal products.

The plans which were launched to increase the world production of food and to improve the distribution of this production are primarily of a more long-term nature, although the nutrition resolution does contain recommendations for concrete short-term measures to assist especially vulnerable groups.

The realizations that the world supply of food will be a cause for concern for many years to come under any circumstances explains the importance given to the third element in the global food strategy: the establishment of a global food security system.

The Food Conference decided to build on the considerable work carried out by FAO in this field in recent years. The conference's endorsement of the undertaking on World Food Security, which the FAO had developed, increased the chances of its effective implementation. The undertaking attempts to make the global supply situation a joint responsibility of all countries through a set of guidelines for storing food, especially grain. The recommendations of the conference imply that one country — the USA — can no

longer hold sufficient reserve stocks for the entire world.

Even if agreement can be reached on such a plan, the physical lack of surplus production makes the creation of such a stock very difficult.

The Conference also agreed to create a global information system which could in-form of impending food scarcities.

The Food Conference considered assurances of guaranteed minimum deliveries of food aid one factor in food security. Agreement was reached to stipulate 10 million tons of grain as such a minimum level. This, together with approval of principles of long-term planning, offers new hope despite the fact that for several years the total amount of food aid has declined while the need has increased dramatically.

However, the Conference did not achieve any concrete results on the organization of international emergency aid, and a proposal to establish an international grain reserve of 500,000 tons for such assistance did not receive sufficient support. Instead an appeal was made to earmark part of national reserves for use in international food emergency situations. At the Conference only Norway and Sweden reacted positively to this appeal. The Norwegian government promised, pending approval of the Storting, to make available 10,000 tons of wheat.

The resolutions of the World Food Conference take the form of requests to international organizations and national governments. A final evaluation of the results of the conference will therefore depend on the ability and will of the individual governments to follow up the approved recommendations nationally and in international organizations.

3.2.4 Follow-up of the World Food Conference and Further Development

3.2.4.1 The World Food Council

In order to assure a coordinated follow-up of the resolutions of the World Food Council, it was recommended to the General Assembly of the United Nations that a World Food Council be created as the central body for food questions and agricultural development. The Council is to report to the General Assembly through the UN Economic and Social Council, which will thus presumably remain the responsible body within the social and economic sector.

The World Food Conference accorded the World Food Council the responsibility for an overall coordination and follow-up of matters concerning food production, nutrition, food

security, food trade and food aid in all UN bodies.

The first session of the new council was held in Rome in June, 1975. It discussed the possibilities of satisfying the developing countries' need for grain, world food security, and the establishment of The International Agricultural Development Fund. Sweden, with the support of Norway, proposed the establishment of an international emergency reserve of 500,000 tons of food to be administered by the World Food Programme.

The results of the first session of the World Food Council were comparatively limited. A relatively general report was adopted, which largely repeated the recommendations and evaluations of the World Food Conference. The hope that the relationship between the Food Council and other UN bodies could be clarified and priorities established for a future programme of work was not realized.

However, in the debate on food questions during the 59th session of the UN Economic and Social Council all members expressed support for the further work of the World Food Council.

3.2.4.2 *The 7th Special Session of the UN General Assembly*

The United Nations in September 1975 called a special session of its General Assembly on Development and International Economic Cooperation to continue the debate on the 6th Special Session of the General Assembly. All resolutions were adopted by consensus. The session also passed a resolution on nutrition and agriculture. It was agreed that the solution of the world's food problems depends on a rapid increase in food production in the developing countries. To achieve this the developed countries must increase their aid to developing countries and at the same time improve access to their own markets for food and agricultural products from these countries. It is also necessary for the developing countries to give high priority to the development of their agriculture and fisheries. A request for sizable contributions to the International Agricultural Development Fund was also adopted.

Another decision of special importance taken by the 7th Special Session was the request for building up food security stocks in developing and developed countries. No direct position was taken on the total extent of the reserves, but it was suggested that wheat and rice should be the main commodities and that these together should constitute 30 million tons.

The special session also approved a request

that all countries earmark food or money as part of an international emergency reserve for use by the World Food Programme. This reserve should consist of a minimum of 500,000 tons of food.

3.2.5 *Evaluation of the Conclusions of the World Food Conference and Views on Future Development*

In this section we will touch on factors which are of special importance for the formulation of a Norwegian nutrition and food policy.

There was unanimous agreement at the World Food Conference that the outlook for the world food supply was very disturbing. The food crisis primarily hits people in the underdeveloped countries. The inequality in the distribution of food which now exists is in danger of deteriorating still more in the course of the next ten years. International cooperation on an extensive action programme was considered necessary in order to avoid a future hunger catastrophe. The food problem must be solved first of all by increased food production in the developing countries themselves. This requires extensive technical and economic help from the rich countries. There will be a very extensive need for food aid in the developing countries for a long time to come. The conference approved a request to the industrialized countries that they exploit their own possibilities for rapidly increasing their own food production. The conference also approved a resolution on the establishment for a system for global food security and an early warning system on impending food scarcities. It was agreed that many countries will be dependent on import of food in the long run as well. All countries were asked to take measures to protect and preserve their food production resources and to reduce the destruction and waste of food. An improved pattern of food consumption in industrialized countries based on nutritional requirements and available resources was discussed on Nordic initiative and recommendations made.

The Food Conference, like many other international forums, advocated rational guidelines for population policy in order to obtain a balance between population and food supply. The limitation of population growth is in all instances a slow process. Even if each woman in the next generation had only one child the population would still continue to increase over the next 30 years, because such a large part of the world population is under adult age. There are few possibilities of reducing population growth to any degree as com-

pared with the prognosed size of the population in 1990, at least in the developing countries. On the other hand, recent development indicates a weaker population growth in the industrialized countries.

Globally, therefore, the food problems in this century must be solved through increased food production.

Many uncertain factors must be taken into account in evaluating the future possibilities for increasing food production. Basic factors involved in the future supply of agricultural commodities are the availability of cultivable land, water, fertilizers and pesticides. Large areas of land under cultivation, with sufficient access to water, fertilizer and pesticides, can produce far more than they do today. It is not a lack of land resources which poses the greatest problem in the developing countries, but the capability for and possibilities of utilizing these in intensive production. If better technology is employed in the developing countries there will be more possibilities of meeting the food requirements today and until the turn of the century. But this will require large increases in the production and the use of chemical fertilizers and pesticides. This in turn will demand strongly increased use of the resources basic to the production of such inputs, including energy (oil). It will also require large investments in irrigation systems, etc. It appears that it will be difficult to achieve a very rapid increase in agricultural production, because the necessary means will scarcely be available. No one can say with certainty how much the world's agricultural area can be increased. Obviously there are considerable land resources. It is also certain that there are no reserves of the extent and quality that there were on the North American continent 100 to 150 years ago. According to all indications the largest reserves of land are in Latin America, Africa and Southeast Asia. Many of these lie in areas with rain forest where there are great problems for both reclamation and cultivation because of precipitation and high temperatures. Furthermore, there are large land areas in arid districts which cannot be utilized intensively because of the low rainfall. FAO estimates that the developing countries can increase their agricultural areas by approx. 20%, or by approx. 1.5 decare for every person by which the population increases between 1970 and 1985. Areas of arable land in the developing countries amounted to an average of approx. 3 decare per inhabitant in 1970. According to FAO's prognosis this will go down to 2.6 decare per person by 1985.

The use of chemical fertilizers and pesti-

cides in the developing countries has increased quite considerably in recent years, but on a per decare basis the consumption of chemical fertilizers in these countries is only $\frac{1}{4}$ of that in the industrialized countries. There is a great scarcity of chemical fertilizers in the developing countries, and prices have risen sharply. It is difficult to predict how much chemical fertilizers will be produced in the future, but few possibilities exist for any great increase in the use. There is also a scarcity of pesticides.

Of the agricultural areas in the developing countries 12% is irrigated, primarily rice paddies. There are considerable possibilities for extending irrigation, but this will require very large investments.

Even if the resources of the ocean have a limited importance in world food production on an energy basis, fish and fish products represent an important share of the protein supply for the world population. As one of the world's largest exporters of fish and fish products Norwegian fisheries are important in this connection. Possibilities seem to exist for a greater exploitation of the resources of the sea, but there are also many uncertain factors.

With a more rational exploitation of resources than we employ today it is estimated that the total annual yield from the sea can be increased from the approx. 60 million tons of recent years to approx. 100 million tons.

According to document E/CONF. 65/3 of the World Food Conference, no more than a 2.6% annual increase in the food production in the developing countries can be expected in the period 1969—71 to 1985. The demand for food is expected to increase by 3.4% per year. The self-sufficiency in food of the developing countries will therefore decrease and the need for imports greatly increase.

The industrialized countries will scarcely expand their agricultural areas significantly in the future. Nevertheless, it is estimated in the above document of the World Food Conference that the industrialized countries will increase food production by 2.8% annually in the period 1969—71 to 1985, while the demand will only increase by 1.7%. The industrialized countries would thus increase their ability to export food to the developing countries, but this increase will scarcely balance the rise in food deficits in those countries. Therefore there are no grounds for anticipating any improvement in the global supply situation in the near future.

As a region the Nordic countries are in a good position with regard to food supply. Denmark, Finland and Sweden have large food production resources. Denmark is a large ex-

porter of livestock products, and Sweden is a considerable exporter of grain. In normal years Sweden will have no problem covering the deficit in grain which Iceland and Norway must anticipate. In addition Finland, Sweden, Norway and Iceland have considerable land resources which have not yet been put to use or are out of use.

In view of the resolutions passed at the World Food Conference and further developments in international forums, the global challenge which face the industrialized countries, including Norway, with regard to nutrition and food supply can be summarized as follows:

- to increase their economic and technical cooperation with the developing countries in order to strengthen and develop food

production in these countries,

- to take measures to protect and preserve their own food production resources,
- to increase their own food production as rapidly as possible with the aim of increasing food aid and export to the developing countries in the short run, and for export to cover the permanent food deficits in these countries in the longer run; nevertheless, these measures must not reduce the opportunities for the developing countries to export their own food products,
- to participate in establishing a system of global food security, and
- to better adapt their food consumption pattern to nutritional requirements and to the food production resources available globally.

Chapter 4. Norwegian Food Supply and Diet

4.1 RELATION BETWEEN PRODUCTION CONDITIONS AND DIET

The diet in Norway varies from area to area, depending on the local resources. There are historical reasons for this which are in the process of disappearing today, but certain differences in the composition of the diet still exist in different parts of the country. For the country as a whole, there are certain special characteristics in comparison with other industrialized countries. More fish is produced and consumed, the same being true for milk and milk products. On the other hand the consumption of meat is relatively low in com-

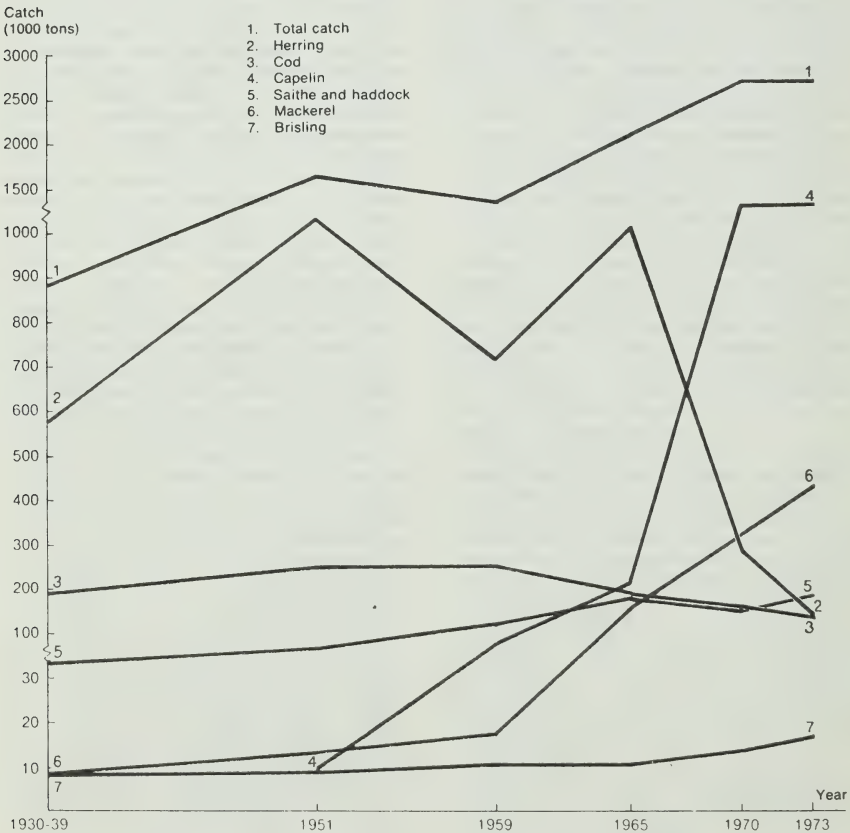
parison with the majority of industrialized countries. The combined consumption of meat and fish is comparatively high. The production of food grain is low in Norway, but the consumption is still in line with that in other western industrialized countries. Sugar is not produced in Norway, but the consumption of sugar is relatively high.

4.2 FOOD PRODUCTION IN NORWAY

4.2.1 Fish

Norway is one of the five largest fishing nations in the world. The total catch has increased from an average of barely 200,000

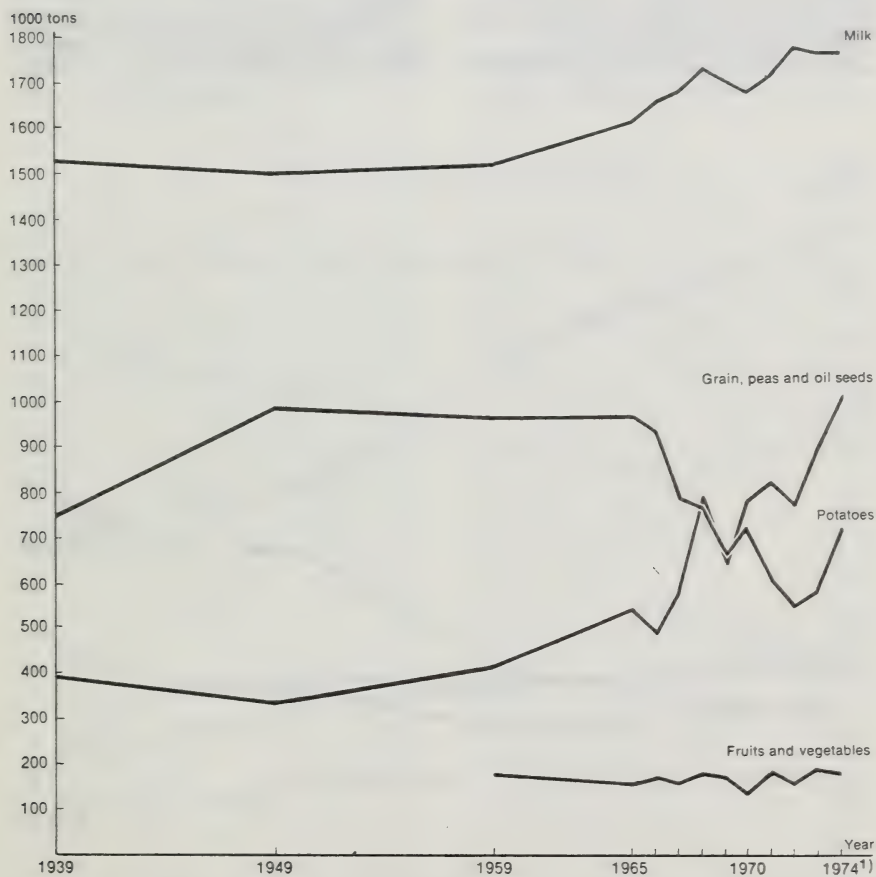
Figure 2 Catches of Important Species of Fish 1930-39-73



tons in the 1930's to approximately 2.7 million tons in the 1970's. However, both the total quantity and the composition of the catch have varied from year to year. The reasons for this have been weather conditions and fluctuations in the fish stocks and migrations. Recent years have been characterized by problems of overfishing and small quantities of important species of food fish. Catches of industrial fish, such as capelin, have made it possible to maintain total quantities, but the proportion of what has been

traditionally defined as food fish has declined from 31% in the 1960's to 22–24% in the 1970's. Figure 2 shows the catch development of important species of fish from 1930–39 up to the present. A decline in the herring catch can be noted, from the peak in 1950 to about 1/10 of that in the 1970's. The cod catch has also declined since the 1950's when catches of about 250,000 tons were taken, in comparison with 150,000 tons and less in the 1970's. The capelin catch, which is essentially an «industrial fish», has increased however, from ap-

Figure 3 Net Production of Various Agricultural Products – 1000 tons



¹) Provisional Figures

prox. 10,000 tons in 1951 to over 1.3 million tons in the 1970's.

It will be a primary task for Norway to help preserve the stocks of fish in order to ensure an optimal production base during the next decades.

4.2.2 Agricultural Products

The available land areas and topographical and climatic conditions limit the production of agricultural products in Norway. This applies especially to grain and sugar beets. In other countries, including Sweden and Denmark, sugar beet is the basis for sugar production. Agriculture in Norway is characterized by cattle breeding because a large part of the land area is suitable for grass cultivation. In central areas grain production has increased considerably in recent years.

The production objectives for Norwegian

agriculture, as stipulated in a report to the Storting (No. 64 1963—64) on agricultural policy, aim at fully meeting the demand for milk, butter, cheese, meat, pork and eggs with Norwegian production. A further objective is to provide full market coverage in respect of potatoes, berries and the coarser vegetables suitable for storing, such as cabbage and carrots. For fruits and vegetables less suitable for storing the goal is to achieve the greatest possible coverage through domestic production.

The objective for grain is to meet as large a part of the demand as is considered reasonable. Livestock production is to be based on Norwegian fodder to the greatest degree possible. There is no plan to produce sugar in Norway.

In Appendix 2 (not translated) a synopsis of the development in the net production of important agricultural products is presented.



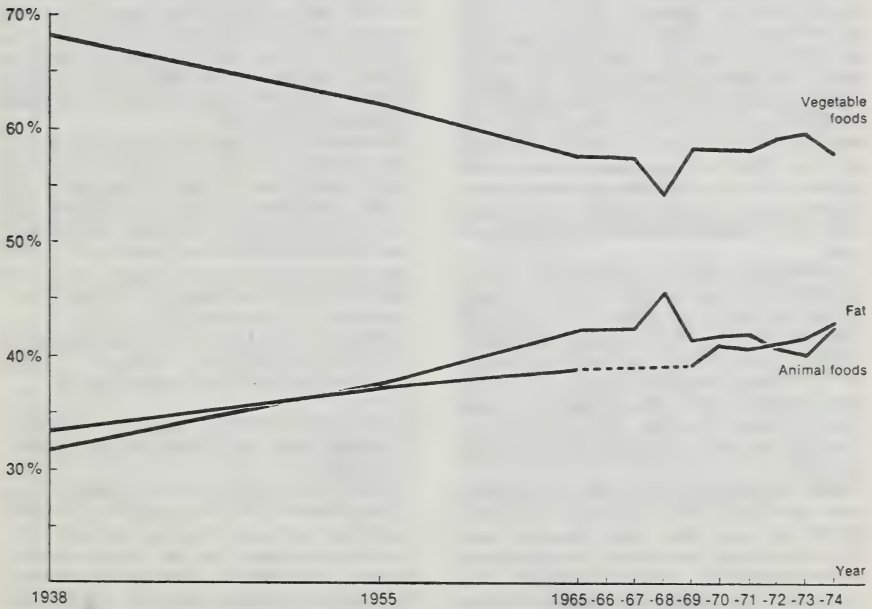
The development in the production of milk, potatoes, grain, fruits and vegetables is shown in fig. 3. It indicates that grain production has increased from 1949 to the present, although there are variations from year to year. Potato production has declined as a result of the fact that potatoes have gradually ceased to be important as animal fodder. Production of fruits and vegetables has been more or less stable, apart from annual crop variations. Development in the production of milk, which is our most important livestock product, shows a more or less steady increase since 1959, although there was a certain decline towards the end of the 1960's. As far as other livestock products are concerned, production has mainly followed the development in consumption, and on the whole the production goals have been fulfilled. One exception which should be mentioned is the production of mutton which has been considerably less than domestic consumption in recent years.

4.3 IMPORT AND EXPORT OF FISH AND AGRICULTURAL PRODUCTS

The Norwegian import of food and fodder is dominated by grain and rice, sugar, fruits and vegetables, and raw materials for the production of feed concentrates and vegetable oils. The grain import varies with the size of domestic crop. In 1973 it was about 879,000 tons, while in 1974 it fell to 713,000 tons. In 1974 the sugar import was about 235,000 tons. The import of fruits has increased steadily and was in 1974 about 186,000 tons, while the import of vegetables varies somewhat from year to year. In 1970 36,400 tons were imported, in 1973 46,300 tons, and in 1974 22,600 tons.

The import of fish has also increased in recent years and was in 1974 about 40,000 tons. It should be noted that a considerable part of the imported fish is used by the Norwegian fish processing industry and is re-exported as processed products. However, export

Figure 5 Percentage Contribution of Various Food Groups Calculated on the Basis of Calories



of fish and fish products is far greater than import, with about 90% of the quantity of fish caught going for export. In 1970 about 338 tons of edible fish were exported, compared to 303,000 tons in 1973 and 262,000 tons in 1974. The export of margarine in 1973 was over 13,000 tons against 10,000 tons in 1974. Cheese is the most important of the agricultural products exported, with about 17,000 tons in the 1970's. This is considered an adjustment export, with a large part of it related to the seasonal fluctuations in milk production, which necessitate a somewhat larger total milk production than would be the case had the production been constant throughout the year. There is a more detailed account of the import and export of important food in Appendix 2 (not translated).

4.4 CONSUMPTION OF FOOD IN NORWAY

Table 4 in Appendix 2 gives a relatively detailed survey of the food consumption in Norway (wholesale level) in kg per person. A general trend in the development is the great stability which is found in food consumption. This would seem to indicate dietary habits and consumption patterns very difficult to change drastically. However, certain changes have taken place in food consumption which are worth noting. Figure 4 shows the development in the consumption of a number of important foods. It indicates that the proportion of cereal products has fallen markedly, but that there are also signs of an upturn. The consumption of fruits and berries has increased considerably. Fish consumption has remained constant over a long period, but since 1970 it has shown a strongly declining tendency. However, some reservations should be taken with regard to the fish consumption statistics since certain corrections have been made which make comparisons over time difficult.

In addition there is the consumption of the so-called «free fish» — fish caught for sport, received as gifts, etc. Figures from a study made for the Fund for Marketing and Distribution Research show that the consumption of «free fish» constitutes about 17% of the total domestic fish consumption, or about 6 kg per person annually. This comes in addition to that which is registered on a wholesale level.

Meat consumption has shown an increase since the 1950's, but this has been more marked the past two years. There is every reason to assume that this is to some extent related to the way consumer subsidies have been used. The largest consumption increase has been in pork.

As far as other livestock products are concerned the consumption of whole milk has been stable, while the consumption of skimmed milk has increased steadily since the mid 1960's. The consumption of butter and margarine has remained relatively constant.

Sugar consumption showed a rising tendency up to 1968, but since then the consumption has fallen off. In 1974 there was a strong decline in the consumption of sugar, which without doubt was connected with the sharp rise in price. It must be noted, however, that there are no figures which show the extent of the increased private trade in sugar carried out by people crossing over to neighbouring Sweden.

When the development in food consumption is examined over a longer period of time it is evident that considerable changes have taken place in the proportion of our energy supply which comes from products of vegetable origin and animal origin respectively.

In 1938 products of vegetable origin contributed about 68% of the energy of the general diet. The corresponding figure in 1968, when this percentage was lowest, was about 54%. This is shown in Figure 5 where trends in food consumption, calculated in calories, are shown. This figure further indicates that the proportion of products of vegetable origin increased somewhat from 1968 to 1973, but fell in 1974. The decline in 1974 primarily resulted from the reduction in sugar consumption. The small increase in the proportion of products of vegetable origin from 1968 to 1973 resulted mainly from an increased use of vegetable products in margarine.

Because of the desired objective to reduce the fat content in the diet, Figure 5 also includes information on the proportion of fats in the total energy supply. It indicates that fat consumption has increased considerably from the early post-war period up to 1974. This has occurred at the expense of carbohydrates, while the proportion of protein has remained relatively constant.

Figure 5 shows that a development towards a reduced fat consumption would be a break in the trends which have prevailed so far.

4.5 CONSUMPTION OF FOOD IN NORWAY COMPARED TO SOME OTHER COUNTRIES

Table 7 in Appendix 2 (not translated) gives a comparison of the consumption of important foods in Norway, Sweden, Denmark, Finland, Great Britain, the USA and the Netherlands in 1971. (Source: Food Balance Sheets.) This survey indicates that our consumption of food floors, including rice, was in the me-

dium range in 1971, while consumption of sugar was somewhat lower than in the other countries. The consumption of fruits was in the medium range, while that of vegetables was low. Our meat consumption was somewhat lower than in the other Nordic countries and much lower than in Great Britain, the USA and the Netherlands. The consumption of fish, however, was much higher than in the other countries. Butter consumption was higher than in the USA and the Netherlands, but lower than in the other countries. On the other hand, the consumption of margarine was higher than in the other countries. The consumption of whole milk was the highest, with the exception of Finland, while that of skimmed milk was much lower than in the other countries. Unfortunately, data are not available on developments since 1971, which makes a comparison between development in Norway and that in the other countries difficult. However, some common development trends can be noted for these countries. When the development in these countries is examined over a longer time period it appears characteristic that the consumption of food flour and potatoes has declined, while the consumption of fruits and vegetables has gone up. There has also been a rise in the consumption of sugar. The consumption of meat has risen strongly, while the consumption of milk in countries other than Norway has shown a somewhat declining tendency.

The consumption patterns which have developed in these countries are typical of those which have occurred in the industrialized parts of the world in the post-war period. An important consequence of this development is that a greater proportion of foods are of animal origin. This in turn requires a greater production of plant material than would be necessary if more products of vegetable origin are to be used directly for human consumption.

4.6 THE DEGREE OF SELF-SUFFICIENCY IN FOOD IN NORWAY

The Budget Committee for Agriculture has assessed the degree to which we are able to cover the demand for foods and has evaluated various methods for measuring this in Appendix 6 (not translated). The appendix indicates that the degree of self-sufficiency in foods, calculated in terms of energy, was 47.7% in 1973. Of this fish comprised 7.5%. When this figure is corrected for the import

of feed concentrates, we find that the proportion of the food consumed in 1973, which came from Norwegian agricultural production based on domestically produced fodder was 31.7%. The reason for this low figure lies primarily in the large energy import in the form of grain and sugar. It should be noted, however, that Norway exports large amounts of fish and fish products. This was referred to earlier in this chapter. Calculated on a protein basis Norway is a net exporter of protein.

Norwegian crop production is characterized by the cultivation of grass. There are climatic limitations for grain production. However, it is possible to increase grain production to a considerable degree. This applies both to food and feed grains. A better utilization of our grass production possibilities, together with a stabilization or reduction in the import of grain, will contribute to increasing our self-sufficiency degree. An increase in root crop production will also contribute to an increase in the degree of self-sufficiency if root crops replace imported fodder.

In 1974 our degree of self-sufficiency in food flour was 6.6%, for vegetables 81.7, and for fruits and berries about 38. For sugar our self-sufficiency is almost zero. In 1973 sugar represented about 13% of our energy supply.

Because of the import of raw materials for the production of vegetable fats, our degree of self-sufficiency in 1973 for margarine was only about 42% and 18% with respect to «other fats». For the other foods such as potatoes, milk, milk products and meat our self-sufficiency was more or less 100%. For mutton, however, the self-sufficiency degree was somewhat lower than for the other types of meat.

4.7 EXISTING PROGNoses FOR FOOD CONSUMPTION

There have been a number of prognoses regarding our food consumption. In Appendix 2 (not translated) one of these is presented, i.e. the Prognosis for Food Consumption 1975-1980-1985. It was prepared by the Budget Committee for Agriculture in 1973 and is based on a number of assumptions, for instance about wage and price developments. The prognosis shows that if the current development trends continue we will not reach the objectives of a coordinated nutrition and food policy as outlined in Chapter 7.

Chapter 5. Norwegian Food Production Resources and Their Utilization

5.1 INTRODUCTION

In Chapter 3 the global supply situation is assessed. An outline is also given of a number of measures which have been put into operation by international organizations, or which have been recommended implemented to improve the international nutrition situation. In this chapter the possibilities which exist for food production in Norway will be examined on the basis of the perspectives outlined in Chapter 3.

The comparatively small areas of agricultural land in districts with relatively favourable climate conditions is a limiting factor for Norwegian food production. The possibilities for Norwegian grain production are of crucial importance to the possibility of increasing the degree of self-sufficiency. In order to make a fairly realistic assessment of our food production possibilities it is consequently very important to evaluate as precisely as possible the cultivable areas.

The data on cultivable areas which we have had up to now are based on the agricultural census of the Central Bureau of Statistics. Because of reasons explained later in this chapter these estimates are very uncertain. An extensive registration of land, which will indicate the areas of arable land, is being carried out by the Division for Land Registration of the Ministry of Agriculture. On the basis of this registration an estimate has been made of the cultivable areas. These figures are presented later in this chapter. It should be emphasized that the figures incorporate considerable uncertainties, and thus must not be regarded as more than a rough estimate. However, they should provide a much better picture of the available cultivable areas than could be obtained previously from the agricultural census. As larger areas are gradually registered the data will be more complete. It is expected that most of the registration will be completed by 1985.

5.2 FACTORS LIMITING NORWEGIAN FOOD PRODUCTION

As noted in Chapter 4, grain, feed concentrates and sugar are the most substantial elements in our food and fodder imports. It is these imports which primarily contribute to the country's relatively low degree of self-sufficiency. The background for these imports are the limited possibilities for sugar production in this country because of the climate and because the areas available for grain production, especially food grains, are very limited.

Limited areas, together with topographical and climatic conditions, restrict what can be cultivated in different parts of the country. The limits are not sharp, nor are they constant over time. They change with different cultivation techniques and with changes in crops.

The mechanization of agriculture has resulted in topographical conditions limiting to an even greater extent than previously the land which can be cultivated. This certainly applies to the cultivation of grain.

In attempting to make an assessment of the resource base for Norwegian agricultural production it is natural to take the crop production potential as a starting point.

Research and development work is of great importance to the possibilities for utilizing the food production resources. Together with the available areas, the yield and the production capability of livestock will be decisive for our food production possibilities.

As mentioned earlier, the limits on what can be cultivated are not absolute. The same applies to the production capability of livestock. Through, for example, crop improvement, the development of improved methods of cultivation and improved livestock the limits will be affected and changed. The most important means of achieving results in these areas will be research.

Agricultural research has long been involved with these problems, and research projects concerned with a better utilization of our food production resources will also be a fundamental task for agricultural research in the future.

The amount of fish which can be taken from the sea depends on the fish resources, the techniques used and the areas which can be fished. So far, our fisheries have covered virtually all our national requirements for fish, and large amounts have been exported. There is no indication that we will not be able to totally cover the country's future need for fish, assuming that resources are properly managed. Some species of fish, however, have been so heavily exploited that the catch has declined, and it must be expected that quotas will be set for the amounts which can be fished of a number of species because of the danger of overfishing.

In order to exploit the opportunities within fisheries there is a general need for an increase in research in this field. It is important to study the resources which form the primary base of our fisheries and to locate and chart possible new ones. The marine re-

searchers must improve our knowledge of the life history of the species, their physical and biological environment, and food chain factors. There is a need for a monitoring which will enable regulation to protect the yield. When new species of fish are to be exploited there must be a thorough study made of their nutritional value and raw material qualities. Thus a reasonable evaluation can be made of the measures necessary at all stages from catch to finished food product. Many species will show considerable variations related to the time and place of catch and to their reproduction cycle. Emphasis must also be placed on research on fishing technology and improved processing.

Product development will be important. At the same time, however, great attention must be given to the nutritional status and quality of fish products for human consumption. This means increased nutrition research and research in the hygiene of food. A better use of the fishery resources thus requires a considerably greater research input.

In addition to the resources in agriculture and fisheries there are the so-called untraditional foods, food production in home gardens, whale and seal catches, as well as the potential in hunting, inland fisheries and wild berries.

5.3 FISH AND OTHER RESOURCES IN THE SEA

The fishing grounds for the Norwegian fisheries cover large areas of the North Atlantic. The main areas for Norwegian fishing, however, are the coastal banks and the adjacent ocean areas. With a potential annual catch of approx 10 million tons, the fishing grounds in the North East Atlantic can be considered the most productive, but also the most exploited, fishing areas in the world.

Norway is the most important fishing nation in these waters, with an annual catch of 2.5—3 million tons. Individual unexploited species of fish and other resources can still be found in the North East Atlantic, such as krill and mussels. However, it would generally be correct to say that the resource base now prevents a further extension of fishing.

The Norwegian fishing industry is based on a wide variety of fish resources and employs versatile catching and processing technology to exploit these resources. This scope in Norwegian fisheries is important in many respects. It provides possibilities for exploiting the resources in the coastal waters, on the banks and in the adjacent open sea areas. This, together with the fact that the fishing

is based on a number of different resources, will have a stabilizing effect on the total production.

In Appendix 3 (not translated) a survey is made of the main stocks for Norwegian fisheries, their total theoretical long-term yield, etc. In the following the most important stocks will be discussed briefly and questions in connection with their utilization examined.

In the Barents Sea, the most important species is the Norwegian Arctic cod. The total average long-term yield of Norwegian Arctic cod, with the fishing methods which have been used in the postwar years, is calculated at about 800,000 tons (whole fish). With more improved methods of fishing the catch could possibly increase to about 1 million tons. However, there are great natural variations in the species, and the catch has varied between 400,000 tons and 1,2 million tons per year.

The Norwegian catch share of Norwegian Arctic cod has varied from about 30% to almost 60% in recent years. Norwegian fisheries are to a large degree based on the exploitation of the spawning cod and are therefore dependent on not too heavy fishing of young cod.

There have long been efforts to get international regulation of the cod fishing in the Barents Sea. A quota agreement came into effect for 1974, but it was terminated by the Soviet Union because the bases for the agreement altered. An agreement for 1975 came into effect in January 1975 under the North East Atlantic Fisheries Commission (NEAFC). The agreement aims at regulations to assure that not too much of the fish is taken in the form of small cod, thereby reducing the total catch, which is especially important for Norwegian fishing. Fishing should also be regulated so that the spawning stock does not become too small to maintain a normal recruitment.

The Norwegian Arctic haddock is another important type of codfish in this area. The long-term yield is estimated at 150,000 to 200,000 tons. The Norwegian catch share has been about 40%. Haddock fishing could also give an increased yield with a better regulation of fishing.

Quantitywise, capelin is the most important type of fish in the Barents Sea. In the course of the 1960's the catch increased from an inconsiderable level to over a million tons, and in 1972 more than 1.5 million tons were caught. So far Norway has almost been alone in this type of fishing, but an increased interest by other countries, especially the Soviet Union, is anticipated. Most of the capelin are fished during the spawning migration in the

winter, but there is also some summer fishing in the northern areas of the Barents Sea.

The northern components of the Atlantic Scandinavian herring are also normally found in the Barents Sea, this species is mainly found in the Norwegian Sea.

Previously this resource yielded an annual catch of over 1 million tons, but it was almost exterminated in the last half of the 1960's. Recruitment was almost entirely absent year after year, while the growing stock was strongly reduced by fishing. The total exploitation pressure on this strain of herring was less, however, than that to which the North Sea herring was exposed in recent years, and the collapse of the stock is probably due to adverse conditions as well.

In recent years a small stock of Atlantic Scandinavian herring has led to a weak new recruitment of the strain. However, it will obviously take a long time to rebuild our winter herring stock to the size it was in the 1950's. A necessary condition for rebuilding the stock of Atlantic Scandinavian herring is a very strict regulation of fishing.

The largest part of the Norwegian saithe catch is taken near the coast and in the fjords, but there is also international fishing for saithe. Of a total quantity of about 200,000 tons in the past few years, the Norwegian share has been about 140,000 tons.

There is a large stock of blue whiting in the Norwegian Sea. These are mainly found scattered over large areas as far as Spitsbergen. The spawning concentrations have recently been detected along the edges of the banks off Ireland and north towards the Faroes and The Shetlands. It is possible that important fisheries can be developed here, since it is considered that the stock is on the same order of size as the stock of capelin in the Barents Sea.

Of the stocks in the North Sea, mackerel and North Sea herring are especially important.

The mackerel was underexploited until the middle of the 1960's but was then subjected to intense ring seine fishing by the Norwegians, which led to an estimated decline in the stock from some 3 million tons to approx 300,000 tons in 1971.

Norway has implemented regulatory measures for mackerel fishing since 1970, which has given the stock a chance to renew itself. It is felt that this resource is now near the level which will give maximum continuing exploitation.

The Irish mackerel, which spawns south and west of Ireland, is not over-exploited and is fished by Norwegian fishermen during the

summer migrations to the northwest part of the North Sea.

In recent years the fishing for North Sea herring has been subjected to a strongly increasing exploitation which has resulted in a drastic reduction of the stock, especially of fully grown herring. As a result the traditional trawl fishing for mature herring has almost completely stopped.

Except for the industrial fishing for young herring, especially on the Bløden Banks, the stock only provides the basis for fishing before and during the spawning season off Shetland, mainly with purse seines.

The total yield of North Sea herring under this form of exploitation was about 500,000 tons in 1973 and only about 250,000 tons in 1974, compared to an estimated optimal yield of about 900,000 tons.

There are also important stocks which provide a basis for Norwegian fisheries in more distant waters. Among the most important are spiny dogfish, ling, cusks, cod and saithe west of the British Isles and off the Faroes and Iceland, and cod, blue halibut and capelin off Greenland and Newfoundland/Labrador. For all these resources, regulations governing exploitation have been imposed or are about to be imposed. In recent years there has also been considerable Norwegian fishing off West Africa. Here the resources are not regulated.

5.3.1 Aquaculture in the Sea

There are two types of aquaculture in the sea. In one the fish take their nourishment entirely or mainly from the natural production of the water. The other type of aquaculture is based on supplying the necessary fodder.

The type of cultivation with supplied fodder has aroused the greatest interest in recent years, and it seems obvious that there are possibilities for developing fish species with a better capability to utilize food under conditions where all the feed is supplied artificially.

This form of fish production can be of great importance in the exploitation of the lower levels of the ocean food chain, such as krill and types of fish, or parts of fish which are in practice not suitable for human consumption. In principle this practice is no different from pork and broiler production, for example, but it appears that the fish can utilize fodder more efficiently.

5.3.2 International Perspectives regarding the Exploitation of Ocean Resources

Internationally we are today in a difficult transitional and adjustment period with re-

gard to the management of the utilization and sharing of fishery resources.

As natural resources the stocks of fish have held a unique position until recent times. Exploitation has been based on principles of common ownership and free competition.

These principles were suitable when fish resources were apparently inexhaustible, as in practice they were until about the middle of this century. Fishing then had little or no effect on the availability of the resources. Today, however, these principles represent a danger both for conserving the resources and for a reasonable exploitation. The rights of the coastal states over the resources in the adjacent sea areas, especially the continental shelf, will be considerably strengthened. With the geographical distribution of Norwegian fishing, where the main emphasis is on the coastal and near-coastal waters, such a legal system will help to ensure the resource base for our most important fisheries in the future, and on the whole will probably result in an increased access to resources for Norwegian fisheries.

5.4 FOOD PRODUCTION RESOURCES IN AGRICULTURE

As mentioned in Section 5.2 the available soil resources are a strongly limiting factor for Norwegian agricultural production. The soil resources consist partly of agricultural areas and partly of areas which are suitable for cultivation. In addition to this there is considerable potential in the outfields and mountain areas.

5.4.1 Development in Agricultural Areas

The development in total agricultural area and fully cultivated area is shown in Figure 6. It shows that the total agricultural area has gone down during the entire period from 1939 to 1974, but it should be noted that the decline was especially great between 1969 and 1974.

The fully cultivated areas increased until 1965, but have since declined. In 1974 the total agricultural area was approx. 9 million decares, which means an agricultural area per person of between 2.2 and 2.3 decares. The fully cultivated area comprises 2.0 decares per person.

Roughly speaking, there are three different ways in which land goes out of agricultural production. It is either taken out of cultivation for various building purposes, structures, roads etc., planted with forest or simply left fallow.

Changes in the agricultural area over time

do not give any complete picture of the size of the areas taken out of agriculture at any given time. This is because of the new cultivation taking place. In Appendix 3 (not translated) the relationship between the decline in agricultural areas and new cultivation has been shown for each county.

From 1969 to 1973, for example, the operated agricultural area in production in this period declined by 825,000 decares, while the total decline in agricultural area in the same period was over 1.2 million decares. Of this area of 1.2 million decares about 77,000 decares were used for building purposes, 4,800 decares were planted with forest, while the remainder, as much as 1.1 million decares, was «used» for other purposes. There is no complete picture of what happens to land which goes out of agricultural production, and which is neither used for building purposes nor forested. Probably a good deal is left lying idle and becomes covered with scrub and underbrush. Under the revised land law the Ministry of Agriculture has started registration work to obtain information of how much agricultural land is unused. Even if this land is not lost as a resource for food production, topographical conditions will make it expensive to bring some of it into food production again.

A positive development trend is that there has been a somewhat steady decline since 1965 in the total agricultural areas which have been used for building purposes. While in 1965 a total of 23,000 decares were given new use under the land law or expropriated and regulated under the building law, the corresponding figure in 1973 had dropped to 11,000 decares. Even though there is a positive trend, and even though the areas which are used for building purposes are small in comparison to the total decline, there is still reason to continue to avoid using productive soil for building purposes. Much of the land which is used in this way, comprises the best soil we have in the country, and the Government considers it very important that these areas are also reserved for agricultural production in the future.

A noticeable trend, which is also evident from Figure 6, is the change in the use of agricultural area which occurred between 1939 and 1974. While the total pasture and grazing area was more than 8 million decares in 1939, the corresponding area in 1974 was down to 5 million decares. The total grain area, on the other hand, increased during the same period from 1.8 million decares to 2.9 million, while the potato area, which reached a peak in 1949, was reduced to half in 1974.

5.4.2 Possibilities for Reclamation

In assessing the possibilities for new cultivation it is worthwhile noting that the concept of cultivable land is ambiguous. Several different criteria can be used as a base. An assessment document (NOU 1974: 55) on «Norway's Resource Situation in a Global Context» mentions three different such basic criteria:

- According to private economic interests.
- From the viewpoint of society as a whole, including food security considerations.
- According to what is technologically possible to cultivate with known technology.

However, there are certain requirements which must apply under normal conditions to areas which are to be cultivated. The soil must be of sufficient depth, must not contain too many stones or rocks, must fulfill certain quality requirements, including moisture, and must not have too steep a surface.

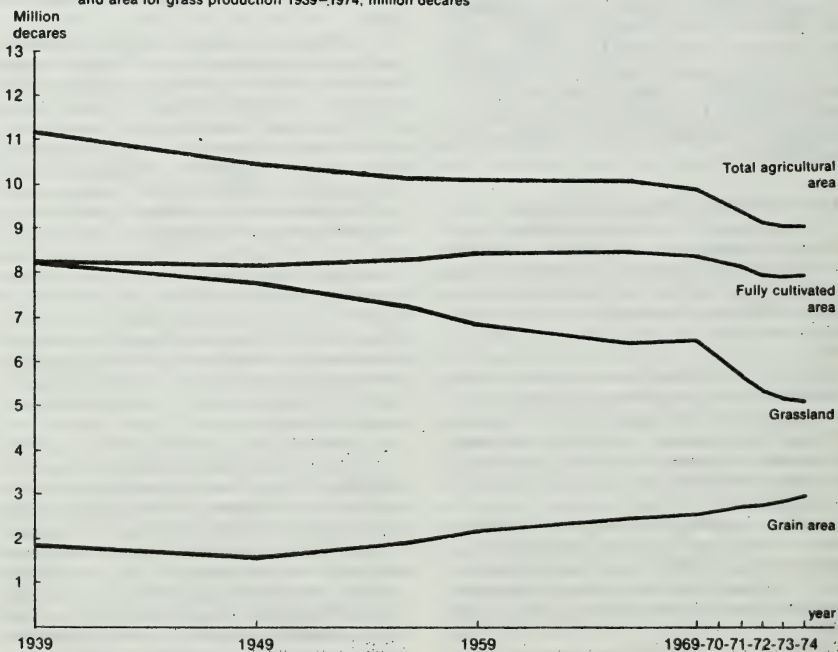
The greatest limitation to the agricultural area in Norway lies in the fact that in many parts of the country there is so little topsoil on the rock bed. In addition, many of the areas with sufficient soil depth are so stony that

it is difficult to use them for ordinary agricultural purposes.

The agricultural census gives a survey of the arable areas, with the exception of those areas not connected with farming, such as land belonging to the state, common land, land under joint ownership and large private forests. The agricultural census survey is based on information given by farmers and includes all areas suitable for reclamation with the technical and economic conditions prevailing at the time of the census. The information is thus based extensively on judgments, in the exercising of which the farmers' own economic situation plays a considerable part. As a result, for example, highly productive woodland may not be registered as cultivable land if the individual forest owner finds it most profitable to produce timber on these areas.

The agricultural census of 1969 indicated that there are approximately 2.2 million decares of land which are suitable for full cultivation in the country as a whole. The more detailed geographical distribution of these areas is presented in Appendix 3 (not trans-

Figure 6 The development in agricultural area, fully cultivated area, grain area and area for grass production 1939-1974, million decares



lated). Because of the factors mentioned earlier in this chapter, there is every reason to assume that there are considerably larger arable reserves in the country than indicated in the agricultural census.

As mentioned in the introduction, the division for Land Registration of the Ministry of Agriculture is involved with an extensive registration of land, which will indicate the cultivable areas. The registration is based on factors such as soil depth, type and quality of soil, amount of stones, and agricultural technical conditions etc. Registration of more than 100,000 km² of a planned registration area of 167,000 km² has been completed, but an overall survey for the country is not available. However, the Division has assessed the available results and on the basis of this has made an estimate of the cultivable area. These calculations are presented in more detail in Appendix 3.

In assessing the arable areas there is reason to emphasize the regional distribution of the land reserves. As mentioned previously, the lack of areas suitable for grain production is one of the most current limiting factors in our food production. Consequently it is of great interest to chart how large cultivable reserves there are in grain districts on the one hand and in grassland on the other. In Appendix 3 the counties of the country have been divided into these two categories. The basis for this is an area grouping presented in Appendix 1 to Recommendation No. 2 (not translated) from the Resource Commission (presented in 1971). By comparing these area groupings with the agricultural census, as shown in this appendix, it is possible to estimate that in the grain districts in S-E Norway and Trøndelag there should be reclaimable areas of 1.8 to 2.0 million decares which can be used for grain production.

In those areas which are primarily suited for grass production there are reserves which are far greater, with an estimated 4–6 million decares below the timberline. This means that there should be arable reserves of 6–8 million decares of good arable land below the timberline, which should provide the basis for a potential agricultural area of 15–17 million decares if all were put to use.

As mentioned earlier, it is not only the total production potential which is of interest, but also the regional distribution. In Appendix 3 an attempt has been made to quantify the potential for grain production, in order to determine the cultivation possibilities in relation to the areas which are used today for agricultural production. Assuming that milk production in the grain districts remains at

about the same level as today, it is calculated that a grain area of approximately 5 million decares is possible according to the area assessments. If meat production based on calves in the grain districts is transferred to grass districts, the estimated possible grain area will be somewhat larger than that which is the case if this meat production remains in the grain districts.

5.4.3 Straw and Outfield Pastures (e.g. rough grazing in outlying areas)

The Budget Committee for Agriculture has carried out an appraisal of outfield pastures and straw as feed resources. The evaluations are presented in Appendix 3 (not translated).

The production of straw has increased in recent years, but only a small part of the crop is used for fodder. In 1974 about 8% or 59 million kg were used for fodder. The rest was ploughed down or burnt.

The fodder value of the straw which was not used for fodder in 1974 corresponds to half the quantity of imported feed concentrates in the same year.

The decline in straw treatment (with alkali to make it more digestible) is connected with pollution problems and increased costs. On the basis of studies made in Norway and other countries it is reasonable to expect that new methods of treatment will again result in an increased use of straw for fodder.

Most of the outfield pastures are in the mountains and forest districts.

The Royal Agricultural Society of Norway has made extensive studies of the fodder resources in mountain grazing in Southern Norway and north as far as Nordland county. The studies indicate that there is an unused capacity in the pasture which were studied, for 1 million sheep. When the unused capacity in Troms and Finnmark is also taken into consideration the total for the country gives an unused capacity enough for an estimated 1.1 million sheep, corresponding to about 100 million feed units.

It is cautiously estimated that the unused grazing in the forest totals 110–170 million feed units.

Not all types of animals are suited to utilize outfield pastures. With the present yields, the fodder basis is usually too poor for milk cows. For sheep, goats, horses and young cattle the fodder base is however adequate. Other conditions, however, limit usage.

On this basis, though, it is reasonable to expect that under normal conditions an increased use of the outfields will first take place in the mountains. Increased use of forest

pastures to any extent can only be expected if there is a scarcity of fodder. The types of animals which will probably be used to graze such pastures are sheep and helpers which are either for slaughter or to be used as future breeding stock. However, caution will have to be taken when grazing helpers on forest pastures.

5.4.4 Possibilities for Increasing Area Productivity

Area productivity, together with the size of the area, will determine the size of the crops which can be obtained. In the calculations by the Budget Committee for Agriculture, presented in Appendix 6 (not translated), there are estimations of area productivity in 1990. In Appendix 3 an account is given of the development in area productivity and the possibilities thought to be present for improvements.

As an illustration of the development which has occurred in area productivity, it can be noted that while the estimated normal annual yield¹⁾ for wheat in 1953 was 220 kg per decare, the corresponding figure for 1974 was 336 kg per decare. For barley the corresponding figures were 249 and 325 kg.

The Budget Committee for Agriculture has estimated the yields per decare for 1990 at 400 kg for barley and 440 kg for wheat.

These figures show an increase in yield of 75 kg barley per decare in 1990 compared to the normal annual yield for 1974, and an in-

crease of 74 kg wheat per decare in the same period. With a grain area in 1990 of an estimated 3.6 million decares the increase in area productivity alone will result in an additional yield compared to the 1974 normal annual crop on the same area, in the region of 270 million kg of grain.

5.4.5 Possibilities for Livestock Improvement

In addition to increased crops per decare, improvements of animal stock are important for obtaining a greater yield from the resource input. In the production of livestock, objectives will be largely based on economic criteria. Such criteria can be quantitative as well as qualitative such as, for example, a greater amount of product per animal, lower consumption of fodder per unit of produced commodity, and production of quality goods in relation to marked demands.

In milk production, emphasis has been placed first and foremost on increasing the milk yield per cow, which has resulted in the yield having increased by about 150 liters per cow per year during the last ten years. There is reason to expect that a similar development will be possible for a number of years to come. How widely such potential will be fully exploited, will largely depend on the extent to which milk production is based on roughage. With limitations on the use of feed concentrates, yields will have to be stabilized at a lower level than would be the case if larger amounts of feed concentrates were used.

Under the system which has so far existed for payment of milk to the producer, there has been a certain incentive to increase the fat content in milk. The National Federation of Milk Producers has plans for paying according to the protein content in milk instead, which would eliminate possible economic grounds for the production of milk with an increased fat content.

The problem, however, is that there is a positive relation between the amount of fat and the amount of solids non-fat (SNF) in milk. Consequently, with selection on the basis of a higher protein content one may also obtain a higher fat content as a result. Despite this, however, it is possible to increase the protein content in milk without increasing the fat content.

Beef production was until recently regarded as a by-product of milk production, and less emphasis was placed on this in breeding than on milk production. This attitude has changed considerably in recent years, in that in both breeding and production a higher meat yield per animal is being aimed at. In the pe-

Table 1. *Normal Annual Yield in 1974 and Estimated Yield in 1990 for some Important Crops. Kg per Decare.*

	Normal Annual Yield 1974	Estimated Yield* 1990
Grain:		
Barley	325	400
Wheat	366	440
Pasture:		
Fully cultivated pas- ture	688	770
Potatoes	2418	2660
Root Crops:		
Fodder turnips and rutabagas	5766	6400

*¹⁾ Calculations from the Budget Committee for Agriculture.

¹⁾ Normal annual yield is a theoretical crop arrived at by extrapolating a straight regression line calculated on the basis of yields (according to the crop statistics of the Central Bureau of Statistics) over a period which includes the crops of the previous year and for as many years back as is desirable.

riod 1960 to 1973 meat production per cow per year, calculated on the total yield from cow and calf, rose from 83.6 kg to 145.5 kg, i.e. an increase of 4.8 kg meat per cow per year. Assuming a continued increase in the years ahead of 4 kg per year, production would reach over 210 kg per cow per year in 1990.

With regard to sheep, the breeding improvement has been considerably slower than for the other domestic animals. However, a better organization of breeding, including cross-breeding with other races, would provide possibilities for progress in sheep breeding as well.

For pigs the number of piglets per litter and the feed conversion rate are the most important economic factors in addition to quality. There has been considerable progress in the use of feed, and there is reason to believe that the amount of feed per kg pork produced will continue to fall.

In egg and poultry production the objective is to lower the amount of feed per kg meat and per kg eggs. The productivity is already good, however, and it appears that additional progress is possible.

5.5 OTHER FOOD PRODUCTION RESOURCES

5.5.1 Food Production in Small Gardens

There is a considerable production of vegetables, fruits and berries in a number of small gardens, but even so only a minor part of the garden and park area is used for food production. The Norwegian Horticultural Society estimates that half of the production of fruits and berries comes from small gardens. On the basis of the figures in the total accounts of the Budget Committee for Agriculture for 1974 the production of fruits and berries in small gardens amounted to about 135 million N.kr. It is difficult to estimate the production area in small gardens, but in Appendix 3 (not translated) an estimate of about 0.4 million decares is made. This comprises about 5% of our fully cultivated area today.

Even though the food production in these areas will be limited in «normal» times, there is reason to suppose that these areas represent a potential which is considerably higher than 5%. In a crisis situation it will be possible to exploit this potential with intensive production so that home gardens and parks can form valuable buffers in periods where great changes in the supply situation occur over a relatively short time.

It is clear that there has been a growing interest in the cultivation of fruits and vegetables in small gardens in recent years, al-

though there are no definite figures for the extent of this. There is therefore reason to believe that more people will gradually gain an increased knowledge of cultivating edible plants, a factor which is important regarding the potential for food production.

5.5.2 Untraditional Foods and Fodder Resources

Untraditional foodstuffs and fodder resources refer here to commodities which are untraditional or new for us in Norway. They could be unexploited products of the land and sea such as, for example, oil seeds, leaf protein concentrates, waste and by-products from animal food production, and fish protein concentrates.

It might be of interest to cultivate micro-organisms for the production of single cell protein for animal fodder, without using agricultural areas.

With available technology it is also completely possible to produce synthetic nutrients, which can be added to and extend more traditional foods.

5.5.3 Whale and Seal Catches

Although the contribution of the whale catch to the food supply plays a more minor role today than in the past, whale meat and blubber continue to be of importance to the food supply. In 1974 the whale catch amounted to approx 548 tons of meat and 847 tons of blubber.

In the years ahead the resource base for a Norwegian whale catch of about 2,000 tons of human food can be anticipated.

Seal meat from the Norwegian seal catch represents a comparatively unexploited food resource.

According to a recent report, a future exploitation of seal meat from Norwegian seal catches could represent about 1,000 tons of boneless meat.

5.5.4 Hunting, Inland Fishing and Wild Berries

Hunting, inland fishing and the gathering of wild berries play an important role in our food supply. The Directorate for Game and Fresh Water Fish estimate that hunting for game meat provides about 2.8 million kg per year. This would correspond to the annual meat consumption of about 60,000 persons. It is further estimated that about 5 million kg fish are caught in inland waters, in addition to 0.9 million kg salmon and sea trout fished in the rivers. There is very little material on the amount of wild berries gathered. The Central Bureau of Statistics uses an estimate

of 4 million kg per year. It is quite clear that there are considerable amounts of wild berries which are not gathered and which thus represent an unexploited resource.

5.6 ECOLOGICAL AND ENVIRONMENTAL LIMITATIONS ON FOOD PRODUCTION

Food production is based, with few exceptions, on the so-called conditionally renewable resources, that is, the biological resources and their production base. **Conditionally renewable** means that the biological stocks must be held at certain levels, and the quality of the production base maintained, if production is to be maintained over a longer period of time. With human intervention the production possibilities can increase or can permanently deteriorate.

The production base for food resources can be impaired in different ways. Productive farm areas can go permanently out of production, for example when used for building purposes, or the production capability of the area can be reduced through impoverishment of the soil, flooding or other forms of poor practices. In the sea, pollution causing a reduction of production capability is the greatest threat to the basis of production.

The biological resources we are dependent on for food production must be managed so that they provide long-term optimal returns. For agricultural production the whole biological process is so regulated that there is no great problem, but for the fisheries, where we only control the catch, long-term exploitation planning is a prerequisite.

In our own waters today the problem complex between the fisheries and off-shore oil production is of specially great interest. Apart from the effect on the national economy, there are two aspects of off-shore oil activity which can lead to difficulties for the fisheries: the areas of the sea which are available for fishing are reduced by structures and pipelines, and the biological production of the sea can be reduced or impaired by pollution. The reduction in available area will hardly result in a reduced total fish production, since nearly all fish stocks are migratory and can be exploited enough, even with reduced methods of catching. But important fishing areas can be lost for a fishing fleet or coastal areas. The pollution effect is potentially the greatest danger.

According to experiences gained in other off-shore areas, significant oil pollution does not result from production under normal circumstances, but from mishaps and accidents. An analysis of the frequency of mishaps in other areas indicates that this is low,

but these circumstances can hardly be transferred directly to our situation. However, it is likely that fishing can be maintained at the same time as oil is extracted from the seabed, assuming that safety measures are extensive enough and that sufficient emphasis is placed on research and monitoring systems. In regard to the sea as a refuse dump, it seems correct to say that the relatively new awareness of the importance of preserving our natural environment in as untouched a state as possible has saved the biological environment of the sea from serious deterioration. Possibilities for successful follow-up of this in the future seems good.

The pollution of land, air and water from other sectors can reduce the production base for agriculture in some instances. Because of unfortunate side-effects of an ecological and environmental nature there will also be limitations on the use of crop-increasing inputs such as chemical fertilizers and various pesticides.

For a more detailed examination of pollution problems reference should be made to a government White Paper prepared by the Ministry of Environment on measures against pollution. It will be presented to the Storting in the Autumn of 1975.

Any significant expansion of the production base in the form of increased reclamation will raise certain economic, environmental and ecological opposition. First, the converting of forest land into farm land means a reduction in the production of timber. The cost of such a change will be greatest in forests with young trees. Secondly, a considerable expansion of the production base for farming through increased reclamation could have unfortunate ecological effects and conflict both the interests of the environmentalists and people interested in outdoor life.

Reclamation is known to have had serious, adverse ecological effects in many parts of the world. The topographical and climatic conditions in Norway prevent reclamation, and thereby changes in nature, from reaching any great proportions, but some of the experiences of other countries should be taken into consideration.

Most important is the effect that the cultivation of former forests can have on the local climate. Forests are wind breakers. Large open areas can lead to wind problems. In the vicinity of residential areas this can reduce the quality of the residential environment. Plant production can also suffer negative effects, because wind increases the danger of drought. The removal of forest can result in cold air from high lying areas drifting down

to lower areas. This can bring about frost damage to crops.

The cultivation of marshland reduces the ability of the area to take up and retain water. This «buffer» effect of marshland is valuable for lowering the flood crest after heavy rains.

Increasing the agricultural area by lowering the water level of lakes can be of interest. In such cases the level of the ground water will be affected. This can be of significance for crop production in nearby higher areas and for the supply of drinking water.

Many of the different types of nature which are potentially most fertile and suitable for cultivation are in themselves of great interest as objects of conservation, in both regional and national contexts, in that the broadest possible spectrum of environments should be preserved.

About half of the reclamation involves marshland. The various types of marsh comprise an important part of the total of nature-types worthy of protection, both from a botanical and ornithological point of view.

Marshes are also of great importance as elements in the landscape and as wild life biotopes. Any great encroachment of these areas will therefore have an effect on more than just the actual swamp area itself. According to a preliminary draft of the national plan for marshy nature reserves it is evident that 3–4% of the country's total marsh area is of interest as conservation areas.

Other wetland areas such as beach meadows, bogs and shallow water areas in both fresh and coastal waters may also be of interest for both new cultivation and conservation. These areas are naturally highly productive and provide an important nutritional base for a rich plant and animal life. The lowering, draining and recovery of arable land in such areas will therefore have consequences. A rich and varied flora and fauna is to a large degree dependent on keeping some of these areas as undisturbed as possible. The importance of such areas to the Spring and Autumn bird migrations should be especially noted. Under the conventions for the protection of wetland areas (the RAMSAR Convention) Norway is committed to the protection of such migratory birds and their natural environment.

From a conservation point of view, the problems of cultivating forest areas are related mainly to forests of certain valuable hardwood species. These thrive better in a warm climate and are to some extent found in areas rich in plant nutrients, which may also be of interest for cultivation. Work is

underway on a national plan for the protection of such forests.

A varied natural environment is also of great importance as the basis for a varied outdoor life and opportunities to experience nature. Increased reclamation in certain areas could reduce the rich variety in nature. The cultivation of further areas will reduce the available area over which the universal right of thoroughfare under the law on open spaces can be practised.

In the concrete plans for reclamation now being developed sufficient consideration must be given to conservation and outdoor life interests.

The areas which merit protection from the angle of conservation are relatively limited, such that the total area which should not be cultivated for this reason is not large.

Because conservation measures do not represent irreversible encroachments on nature, the possibilities for cultivating areas which are being protected will not be lost if there should later arise a situation where cultivation is felt to be absolutely necessary.

5.7 SUMMARY AND CONCLUSIONS REGARDING POSSIBILITIES FOR FOOD PRODUCTION IN NORWAY

The estimates outlined in the above section indicate that technically and biologically there are considerable possibilities for increasing Norwegian food production.

The contribution of the fisheries to food production will depend on several factors which are discussed in more detail in Section 5.1. Assuming a destructively heavy exploitation can be hindered, there is nothing to prevent the fisheries contributing at least as much to Norwegian food production in the future as they do today.

For a country like Norway the supply of grain for both food and feed will be of vital importance to the food supply situation. On the basis of the calculations made earlier in this chapter, there should be possibilities, calculated purely technically/biologically, for a Norwegian grain production in 1990, minus seed and waste (46 kg per decare) of approximately 1.8 million tons. Assuming a population of about 4.2 million in 1990, this will correspond to about 470 kg per person per year. This means that the import of grain could be reduced to a minimum.

If it is further assumed that some of the feed concentrates which are used today in livestock production will be replaced by Norwegian roughage, the import of grain and feed concentrates could be totally replaced by

Norwegian fodder. An assessment of the resource base seems to indicate that there should be nothing to prevent this.

The limitation for Norwegian food production, on a technical/biological basis, will lie more in the selection of different plants than in the production of the necessary food energy. Under all circumstances we must expect to import the sugar we require, as well as some fruits and vegetables. As far as fruits and vegetables are concerned, the import will be related to the selection we desire and to whether a supply is required throughout the entire year.

On the basis of the above it can be concluded that it will be technically/biologically possible to limit our import of food primarily to sugar, some grain, some fruits and vegetables and some vegetable fats. This applies even if our present consumption pattern is maintained. It must be emphasized that no consideration has been given in the calculations made here to the side-effects which such a large-scale cultivation, as has been assumed, would have. If it is assumed that about 1 million decares of the arable land is high quality forest, one consequence will be a future annual decline in forestry production of an estimated 0.5–1.0 million m³ lumber. Furthermore, as mentioned earlier, harmful ecological and environmental effects cannot be excluded. Thus the calculations do not indicate which type of production resources can be reasonably used for food production, but they attempt to give an evaluation of the biological/technical limits for Norwegian food production.

5.8 UTILIZATION OF THE FOOD RESOURCES

In the preceding sections of this chapter an attempt has been made to give a perspective of the potential for primary food production in this country.

In assessing the supply of food the extent to which primary food production is used for food and how much loss there is between primary production and finished food products must also be considered. Less waste will be just as important as increased primary production in increasing the supply of food products from Norwegian production.

5.8.1 Use of Fish and Fish Products

The food products from the sea are valuable first of all as a source of protein. They cover in human nutrition on a global basis only 1% of the energy requirement. However, they provide about 11% of the animal protein.

About one third of the world catch, or ap-

proximately 20 million tons of fish, is used for the production of fish meal and marine oils. The oils, are mainly refined for direct human consumption purposes, but all the fish meal practically speaking is used for livestock in feed supplements.

Two-thirds or more of the Norwegian catch goes for such purposes. This use of a commodity, which in principle is a high value food, is often the subject of discussion. At present there is no real choice between using the fish directly for human consumption or as animal feed.

So far it has not proved possible, for technological, economical and marketing reasons, to produce acceptable food fish from Peru's 10 million ton catch of anchoveta nor the Norwegian catch of 1 million tons of capelin. Processing of these commodities must be given higher priority, however. Until a better use for this fish is found it will be no misuse of resources to use it for animal feed. On the contrary, to allow a renewable resource to simply exist, without utilizing it, would be a waste, as opposed to what would be the case with non-renewable resources.

In recent years there has been an attempt to produce and market fish meal, usually called fish protein concentrate (FPC), for human consumption. If the production and marketing of this product is successful it could be of the greatest importance both from a resource use and nutrition points of view. Fish is a very perishable commodity, and preserving, freezing and other processing considerably increase the cost of the products. This in turn results in an inequality in the distribution of fish products, with the rich countries, which already have an unnecessarily large consumption of protein getting more than their fair share. Low priced fish meal or equivalent products which could be used both to give taste and as a nutrition supplement could result in a better distribution of fish products in relation to the nutritional requirements and could mean that as yet unexploited resources in the sea at lower levels in the food chain could be used. This again could result in a considerable increase in the potential of the sea for food production.

The proportion of the Norwegian catch consisting of edible fish — that is to say, fish used for human consumption — has declined from 31% in the 1960's to 22–24% in the 1970's. This is because of a large expansion in the industrial fisheries in this period.

The percentage decline does not imply, however, that the absolute amount of edible fish available thus far in the 1970's has been less than in the preceding decade. On the

contrary, there has been a certain increase in volume (3–4%).

If a greater consumption of fish is desired, it is necessary to present a broader choice of foods with a fish base or with fish as one of the ingredients. It is therefore important to encourage research related to raw materials and product development.

Considering the limitations which the fishery resources themselves set for Norwegian fishing, an important objective is now to find products and production methods which can result in a larger part of the total Norwegian catch being used directly for human consumption. The Government will attempt to assist in such a development.

5.8.2 Utilization of Important Agricultural Products — Use of Household Wastes

The calculations for food consumption given in Appendix 2 (not translated) indicate that the average consumption of food on the wholesale level per person per day is about 3,000 cal. Other estimations based on the theoretical physiological human requirements, together with an evaluation of the structure of the population, indicate the average food consumption to be 2,500 cal. per day.

According to a research report on the use of waste from food production and consumption, produced by the Chr. Michelsen Institute for the Commission on Solid Waste of the Norwegian Council for Scientific and Industrial Research, the waste which occurs between the wholesale level and actual food in-

take is calculated at 16% of our food production.

In this research report a more detailed examination is made of the utilization of three important commodity groups, namely food grains, and dairy and meat products. Together these cover more than 50% of our food energy supply.

It is noted in the report that with an improved utilization of the offal of slaughtered animals it would be possible to produce an extra 15 billion calories for human consumption. This corresponds to the food energy content of 35,000 slaughtered pigs. Furthermore, about 6,700 tons of flour or about 23 billion calories are lost to human consumption in the form of stale bread which is returned from bakery shops.

It is obvious that a greater part of these food resources could be used for direct human consumption. In Norway the level of utilization of by-products from slaughtering is low compared to that in Sweden and Denmark. This is probably due to different eating habits, but it can also be assumed that the level of product development within the food industry can have a vital influence on utilization.

A considerable part of the waste in by-products, however, is utilized as animal feed. To the extent the feed is used for food producing animals many of the by-products and much of the waste are thus used for food via livestock. However, there is a considerable amount of by-products and waste which is not utilized at all. Of no small importance in

Table 2. *Sources and Types of Waste*

Source of Waste	Type of Waste	Amount tons per year	Feed value 1000 feed units per year
Private households	food refuse	270,000	70,000
Catering establishments, canteens	food refuse	40,000	10,000
— including			
Hotels + restaurants	food refuse	(15,000)	(4,000)
Hospitals	food refuse	(10,000)	(2,600)
Bakery shops	bread products	6,700 (as flour)	6,700
Slaughter houses	blood intestinal contents	2,680 28,700	600 —
Dairies			
— receiving stations	rinsing water	10,000 (as whole milk)	2,000
— cheese factories	waste whey surplus whey	29,000 185,000	2,000 12,500

Source: Research report on use of waste from food production and consumption. Chr. Michelsen Institute.

this connection is the utilization of vegetable and animal matter from household wastes. It is thought that pigs are the most effective utilizers of this part of household waste.

The total loss in the dairy industry in 1973 was about 97,240 tons calculated as whole milk. This comprised 5.83% of the total amount of milk delivered to the dairies. Almost $\frac{2}{3}$ of the loss was surplus whey which was dumped. The rest of the waste was lost in production, especially in the cleaning of equipment.

The dairies are making intense efforts to find a solution to the whey problem. Among other things, whey is a possible substrat in the production of single cell proteins.

Table 2 gives a survey of the amount and composition of waste from different sources. The table shows that the waste included here represents a feed value in excess of 100 million feed units per year. This corresponds to the feed value of about $\frac{1}{5}$ of the Norwegian grain production in 1974.

It should be stressed that a utilization of this waste as animal feed would involve many problems. These are hygienic, technical, economic and organizational. With greater research inputs on the utilization of these resources, together with greater profitability for the producers through using Norwegian feed, it should, however, be possible to exploit a good deal of the waste in a better way than is the case today.

More detailed assessments of the utilization of fisheries waste, food and other wastes are described by the Commission on Recycling which has presented two reports:

NOUR 1973: 51 «Recycling of Treated Waste»

NOU 1975: 52 «Recycling of Treated Waste II»

5.8.3 Industrial Processing

Food supply has become the subject of industrial processing to an increasing degree. Radical changes in both production and distribution have taken place since the last war. The focal point in the processing of food has shifted from the household to the food industry.

Previously, a large proportion of food products was offered and sold within a short time in the immediate vicinity of the place of production. Markets have expanded considerably in the past 20 to 30 years and are today nationwide and more international than before. At the same time, a concentration of processing has occurred, and the size of the production units has increased.

Food is now transported over longer distances and stored for longer periods.

The demand for completely processed foods and other new products has increased.

Development has been away from personal service stores and the sale of unpackaged goods to the sale of pre-packaged food products in self-service shops.

One basic reason for this development lies in the scientific and technical progress which has made the introduction of new methods of processing, packaging, preserving and keeping foods possible.

5.8.3.1 Effect of Industrial Processing on Nutritional Content

Industrial processing can often result in the finished product having a different nutritional composition than the original product. Certain elements can be removed and the product becomes poorer in nutrients. The grinding of grain is an example of this. The external part of the kernel, which is richer in minerals and vitamins, is removed and used as animal feed, and the flour is poorer in these nutrients than the grain itself.

Some raw materials are fractionated, and the nutrients distributed between different products, which thus have a different nutritional content than the raw material. An example of this is cheese production. Here the least soluble protein in milk, casein, goes to cheese, while the more water soluble proteins and other water soluble nutrients remain in the whey. This is either used in other production or is thrown away.

During processing food will often go through processes which break down the nutrients and thereby reduce their amount. This occurs first and foremost when they are exposed to heat, as in cooking, parboiling, autoclaving, drying, etc. Other factors can also cause a breakdown, such as light, washing, acid or lye treatment, aeration which can accelerate oxidation, or contact with metals which can accelerate catalysation and lead to undesirable deterioration in taste and quality.

Often several factors work together. The nutrients which are most easily affected are protein, fat, and vitamins. An end product can therefore have a different and poorer nutritional content than the raw material even if none of the components are removed. The same factors can also influence other quality characteristics such as taste, smell and consistency.

The preservation methods used most often in Norwegian industry today are deep-freezing, canning and drying. Of these deep-freezing is the method which best maintains the original qualities of the food.

However, in individual instances processing can lead to a better utilization of nutrients. The treatment can increase the digestibility of the product, making the nutrients more available to the human organism. An example is proteins in legumes, which are better utilized after mild heat treatment which removes certain inhibiting materials which lower the digestibility of the proteins.

5.8.3.2 *Enrichment of Foods*

The addition of one or several nutrients (usually vitamins or minerals) is carried out in varying degrees in different countries. The purpose of enrichment is:

- To compensate for nutrients which are lost in the processing of foods.
- To bring the content of certain nutrients in substitute foods up to the level of the content in the commodities they imitate.

- To ensure that the population receive a reasonable supply of nutrients which it is felt might otherwise be lacking.

5.8.3.3 *Food Additives*

Food additives are chemical substances which are added either as preservatives to extend durability by hindering microbiotic and chemical transformations or to improve appearance, consistency, smell and taste of food products. It is especially the centralized production of pre-packaged food products which has led to an increased use of additives.

Because of possible harmful effects to the health of the consumer, the use of these substances is subject to control by the health authorities, and only additives which have been approved by the health authorities can be used. The Directorate of Health limits the use of additives as much as possible.

Chapter 6. Factors which influence Diet

6.1 INTRODUCTION

The consumption of food is influenced by a large number of factors. It is difficult to survey all of these, nor can it be said definitely what significance the various factors have. This will vary from consumer to consumer and between the different types of household.

This chapter will therefore be limited to a discussion of a number of factors which are felt to be of importance, and there is an attempt in Figure 7 to present an outline of the main factors which affect the diet. The individual factors and groups of factors influence each other reciprocally, so that it is difficult to delimit definite individual causal relationships. Resources, primary food production, and to some extent industrial processing are examined in more detail in previous chapters.

Factors which influence consumption can be divided into two groups. The one group includes factors beyond the control of the individual consumer, such as individual food

prices, the relationship between the prices of different foods, and the choice of foods normally available to the consumer.

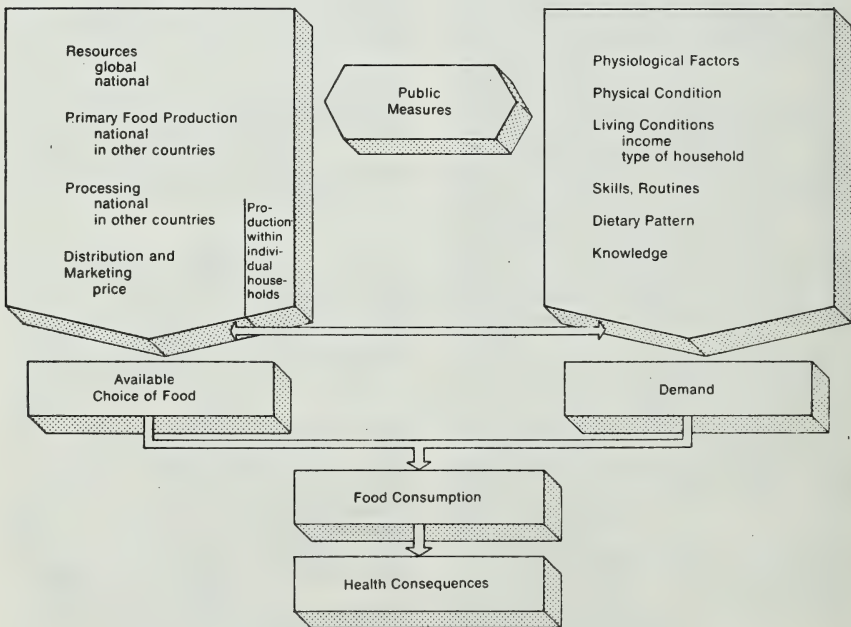
The other group includes factors which have a more direct connection with the consumer or the household, such as the size and composition of the household, income, knowledge and skills, dietary pattern and preferences.

6.2 FACTORS BEYOND THE CONTROL OF INDIVIDUAL CONSUMERS

With the transition to a monetized economy and the expansion of the retail food trade, it is now usual to base the diet on purchased foods. Today the majority of households can plan their diets with less dependence on local food production than previously. Even in large food producing areas, increased specialization has led to a dependence on food shops.

The available choice consists partly of domestically produced goods and partly of imported goods. Products are presented to the

Figure 7 FACTORS INFLUENCING FOOD CONSUMPTION



consumer in definite ways, prices and marketing measures having perhaps the greatest influence. Production which takes place within the individual household must also be taken into account.

6.2.1 Import

Norwegian imports and exports are based on trading patterns and conditions developed through international cooperation, as expressed in GATT, the EFTA convention and the EEC trade agreement. As a participant in this cooperation, Norway has accepted limitations, on a reciprocal basis, on her freedom of trade. The limitations imply, among other things, that Norway cannot employ certain trade policy measures, e.g. a quantitative regulation of the import of commodities included in the agreements. Further there are many tariff rates determined by GATT which cannot be raised without negotiation. An important principle in GATT is that discrimination is not permitted between the contracting parties. This principle can be departed from when it applies to the tariffs on imports from developing countries. In addition, Norway will probably gradually achieve so strong a currency position that other countries will expect her to conduct a policy favourable to imports in the food sector.

In 1973 Norway imported food products worth 2,411 million N.kr. which corresponded to 7.2% of the total import excluding ships. About half of this comprised fruits and vegetables and grain and cereal products.

The import of food products limits the possibilities for the sale of Norwegian produced food products thus affecting the choice available to the consumer.

According to Appendix 6 prepared by the Budget Committee for Agriculture, Norway imported 52% of her food requirements on an energy basis in 1973, or 61% when the amount of energy in livestock products based on imported feed concentrates is taken into account.

For further information see Appendix 4 prepared by the Ministry of Trade (not translated).

6.2.2 National Production

Food production in Norway is discussed in Chapter 4.

The types of goods which producers and distributors choose to concentrate on within the individual product groups, or in other words the types of vegetables, meat, and cereals etc. it is decided to produce most of, will have an important influence on food consumption patterns. The framework for this production is partly set by consumer de-

mand, and partly by import regulations, agricultural policy measures, production conditions, and developments in plant and animal breeding.

Industrial processing of primary foods is very often necessary. Food production usually takes place far from where the majority of the consumer live. One or another form of preservation is therefore necessary to ensure that good quality products reach the consumer. Seasonal production, especially of vegetable products, and to a certain degree overproduction in certain periods also make it necessary to preserve foods, or to make provisions for proper long-term storage.

Processing on an industrial scale offers a number of advantages, among the most important being that industry takes over many time and energy consuming tasks otherwise performed in the home. The industrial processing of foodstuffs also confronts us with such problems as the choice and composition of products not corresponding adequately with nutritional considerations and/or that some production processes are based on a poor utilization of raw materials.

6.2.3 Distribution

Food products reach the consumer through a well-developed distribution system. At the same time a number of marketing measures are employed in order to ensure a demand.

Little attention has been paid to the effects changes in supplies and distribution of foods have on the diet. It can be said, however, that two elements play a role:

- which foods are available, and
- marketing measures introduced to influence the demand for food products.

The trade in foodstuffs has become steadily more businesslike. Larger wholesale and producing units and the expansion of economic administration systems, based on modern computer techniques, have resulted in all the links in the distributional system becoming more cost oriented. This may result in products which sell poorly being sifted out.

The demand for a more effective distributional system can result in larger producers and retailers gaining an advantage over smaller ones. The quality and composition of foods are assessed according to business criteria.

Structural changes in the retail food trade have occurred rapidly in the postwar period. First there was the change-over from «manual» to «self-service» food shops, and then gradually a change-over from many small grocery and specialty shops to fewer and larger stores and department stores.

According to the Central Bureau of Statis-

tics, the number of food retail outlets declined by 3,850 from 1963 to 1973. There were almost 13,000 retail outlets in 1973. From 1952 to 1963 the decline was limited to about 100.

This structural rationalization may have certain favourable consequences in densely populated areas but may present problems in more remote areas. Increased distance between the home and shop can also lead to problems for certain consumer groups in densely populated areas, such as the elderly and functionally handicapped.

The retail food trade in outlying regions is examined in Appendix 1 to a Government report (St. prp. Nr. 1 for 1975—76) prepared by the Ministry of Trade and Commerce. In this report support measures are proposed for maintaining the necessary services.

Experiences in Sweden indicate that meat products, preserved and deep frozen products, and fruits and vegetables increase their share of the total turnover with increasing shop size.

This development is thought to have opened possibilities for an improved range of foods in the individual shops, especially of processed fresh products.

Food shops are subject to local authority closing by-laws, which usually stipulate closing not later than 6 or 7 p.m. on weekdays. This means that the consumer has few opportunities to shop for the necessary goods such as bread, milk, sandwich foods, dinner foods, etc. after a certain time of day. On the other hand, goods such as various sorts of snacks, chocolate, cakes, fruits and soft drinks are more easily available from newsstands, cafeterias etc.

6.2.4 Marketing Activity

Today's marketing offers producers and distributors a number of opportunities for influencing consumer demand. Marketing is becoming steadily more tied to brand products. Attempts are made to promote the turnover in brand goods through advertising, product development, packaging and sales help to the retailer. A survey of brand name advertisements for foods will therefore give an indication of which foods are being promoted at any given time.

Norwegian Advertising Statistics A/S produces annual statistics on expenditure for food advertisements in the daily press, weekly magazines and trade periodicals. The statistics cover almost all brand name advertising in this field.

In 1974 the cost of food advertising was almost 32 million N.kr. and corresponded to 9% of the brand name advertising that year.

The largest part of this advertising expenditure involved the following product groups:

- Chocolate, sweets, cooking chocolate, chocolate milk powder, etc.
- Meat, meat products.
- Butter, margarine.
- Carbonated soft drinks containing sugar, fruit squash, juice.
- Ice cream, desserts, cream, sour cream, eggs.

Marketing of foodstuffs is also conducted through special advertising leaflets, displays in shops, posters, packaging, reduced prices, demonstrations, etc. Commercial advertising comprises a large part of total consumer information concerning products and product range.

From a nutritional point of view this advertising is often lacking in important aspects. For example, products are seldom presented within the framework of a wholesome and suitable diet. Similarly, practical instructions for use from the producer are not always nutritionally appropriate.

The Consumer Ombudsman has handled a number of cases under the marketing act, which have consequences for the marketing of foodstuffs. Among other things, specified requirements have been drawn up for the marketing of products for «slimming diets». Also voluntary agreement has been reached on the placement of sugar and chocolate products in food shops.

It is difficult to draw conclusions as regards direct relationship between marketing measures and consumption. However, a large sum is spent annually on marketing measures and it must be assumed that, on the whole, this sum is well spent according to trading objectives. In other words, experience and information indicate that this input influences demand in the anticipated direction.

6.2.5 Prices and Subsidies

6.2.5.1 Prices and Incomes as Factors Influencing Consumption

An important factor which influences the demand for a product is the price. For the majority of products demand falls with rising prices, and rises with falling prices.

How strongly demand will react to a price change is dependent on several circumstances, including the degree of the price change and the consumer's income.

The so-called demand elasticity is often used as a unit of measurement for the different factors influencing demand. This can be divided into price elasticity and income elasticity.

Price elasticity expresses the percentage

change in the demand for a product when the price of the product changes by one percent. Price elasticity is usually less than zero, i.e. the demand for a product goes down when the price increases. Income elasticity expresses the percentage change in the demand for a product when income changes by one percent. For most goods, income elasticity will be greater than zero, i.e. consumption increases with increased income. The consumption of some foods will increase with increasing income, while the consumption of others will fall.

The third type of elasticity is cross elasticity which is expressed as the percentage increase or decrease in the consumption of a product when the price of another product changes by one percent.

Elasticity figures are valid for moderate price changes, and they will remain constant over a limited period of time. It is of interest to note both the levels and development tendencies of the different elasticities.

Generally it can be stated that demand elasticities for foods are on the whole low. That is to say, moderate changes in price and income conditions cause moderate fluctuations in the demand for foods. This is related to the fact that foods satisfy basic needs, which must be covered before individuals begin to demand other goods and services.

This applies to foods as a commodity group. If we examine the individual foods we find considerable variations.

Some of the studies on the size of demand elasticities for foods were made quite some time ago and the material on which calculations are based is often too sparse to provide accurate up to date figures. A more detailed examination of fluctuations in the demand for individual goods will be made below on the basis of calculations carried out by the Budget Committee for Agriculture.

Cereals, potatoes and milk are commodities which have very low demand elasticities. As far as price elasticity is concerned, calculations indicate elasticities close to zero. Demand is thus relatively independent of price. As has been shown in previous chapters, the consumption of cereals and potatoes has declined in most industrialized countries. This has occurred concurrent with an increase in personal after-tax income. This suggests that the demand for these products declines with increased incomes. The Norwegian calculations indicate this as well. As far as milk is concerned, however, this is not the case.

Skimmed milk also has a price elasticity of approximately zero, while the calculations made for this product indicate that consump-

tion increases with increased income. The consumption of sugar does not appear to increase further with rising incomes. This is very probably connected with the income level we have in Norway today. Some years ago the situation would probably have been the opposite.

Meat and pork are examples of products with somewhat larger demand elasticities than for cereals, potatoes and milk. Calculations made in 1974 indicate a price elasticity for pork in the order of ± 0.3 to ± 0.7 , and for beef in the order of ± 0.8 to ± 1.1 . The income elasticities are estimated at 0.4 to 0.6 and 0.5 to 0.8 respectively. These figures indicate that the demand for beef is more price dependent than for pork. Changes in the price relationship between these types of meats will have an influence on reciprocal demand. The calculations imply that changes in the price of pork have less effect on the consumption of beef than the reverse.

For fruits, berries and vegetables there are great variations within the groups. Generally it can be said that vegetables such as cabbage and carrots have a low demand elasticity while tomatoes, for example, appear to have a relatively high demand elasticity. It should be stressed however that there is little recent material on this.

Calculations have been made for fish which show a relatively low price elasticity and low income elasticity. It seems, however, that meat and fish are to a certain degree alternative products, so that changes in price relationships are just as significant as changes in absolute prices. However, there are few calculations which show the cross elasticity between these goods.

6.2.5.2 Price Levels and Use of Price Subsidies

Price trends and the general price level for foods have been strongly influenced through the years by price and subsidy policies followed by the authorities.

The primary objective of these policies has been to control general price trends in the society. It has not been the aim especially to influence levels and relative prices of individual food products. The distributional aspect of the measures, i.e. concern for economically weak households, has also carried great weight. For this reason subsidies have mainly been applied to foods which weigh heavily in the budget of the ordinary family.

In recent years, subsidies have been important tool in price and distribution policy. Table 3 shows amounts paid in consumer subsidies and as compensation for value added tax on foods from 1970 to 1975.

The foods which are subsidized today are primarily milk and milk products, flour, meat, fish and fish products and margarine. In 1975 the subsidy was distributed so that roughly half went to milk and dairy products.

Table 4 shows the allocation of subsidies as of November 1, 1975.

The direct maximum price regulation covers only relatively few types of goods, including milk and cream. For meat and pork and for meat and sausage products the calculation rules for price quotations by the Prices Board for Meat and Sausage Products apply. Separate price ceiling regulations apply to margarine and edible fats from factories. For butter and cheese, flour and grain (grits), and for feed concentrates, there is an arrangement prohibiting a rise in wholesale prices without consultation with the price authorities.

One result of subsidization and price regulation is a shift in the relative prices.

It must be assumed that the consumption of subsidized foods is greater in most cases

Table 3.

Amounts paid in consumer subsidies and compensation for value added tax on foods, 1970 to 1975.

	Subsidies Million N. kr.	Compensation for Value Added Tax Million N. kr.
1970	601.8	
1971	641.0	
1972	645.0	
1973	847.7	
1974	1,230.8	509.0
1975	1,354.4 ¹⁾	746.1 ²⁾

¹⁾ Appropriated.

²⁾ Estimate.

than would have been the case without subsidies. Subsidization will therefore affect the pattern of consumption and can to a certain degree be used to influence the consumption of selected foods.

Table 4.

Rates for subsidies and compensation for value added tax, 1975. Øre per kg/liter.

Commodity	Subsidies	VAT compensation	Total
Whole milk	111.7	23.0	134.7
Skimmed milk	94.9	15.0	109.9
Cheese, average	271.0	200.0	471.0
Butter	48.0	182.0	230.0
Flour, average	108.6	21.0	129.6
Margarine, average	106.0	87.0	193.0
Meat from cattle, calves and reindeer	176.0	254.0	430.0
Meat from sheep and lambs, goats and kids	331.0	254.0	585.0
Meat from pigs	—	165.0	165.0
Fish incl. herring unprocessed		140.0	140.0
processed		277.0	277.0
Whale meat		277.0	277.0
Frozen fish unprocessed		140.0	140.0
processed		277.0	277.0
Frozen whale meat	—	277.0	277.0
Canned dinner foods based on fish and whale meat ..	—	190.0	190.0

6.3 FACTORS RELATED TO INDIVIDUAL CONSUMERS

6.3.1 Types of Household

The largest consumption of food takes place in private households. The 1970 census showed that there were almost 1.3 million households in Norway. These were defined as «dwellings for one or more persons with common meals and lodging».

Geographically, considerable differences must be expected in opportunities for the

self-production of food. Different households also have different possibilities for keeping and preparing food. In households with poor preservation and preparation facilities, there is a greater degree of dependence on finished products and certain other products which are easy to prepare. This limits the possibility of preparing a more varied diet.

The size and composition of the household will to a certain degree influence the diet of individual members of the household.

Table 5.

Large Households Serving All Daily Meals

	Number	Number of	Average beds	Total
		beds	per institution	
Health institutions ¹⁾				
General hospitals	203	21,262	105	
Special hospitals	86	15,360	179	
Convalescent homes	398	13,941	35	
Convalescent and old age homes (combined) ..	280	12,346	44	
Old age homes	489	11,681	24	
Rehabilitation institutes	62	2,456	40	
Convalescent hotels	7	249	36	
Total number of beds				77,295

Other Large Households Under Public Responsibility¹⁾

Armed Forces	111	27,190	245	
Prisons	12	1,480	123	
Student Hostels ²⁾	400	21,788	54	50,458
Total number of large households for which the authorities are responsible		127,753		

¹⁾ Training of Personnel in Large Households,
Report - NOU 1975: 36.

²⁾ Student hostels include:

Folk high school	79	institutions
Elementary schools	100	"
Special schools	45	"
General high schools	12	"
Occupational and trade schools	80	"
Other boarding schools	86	"
Total	400	institutions

In addition there are the meals served to the
crews of the fishing fleet and of ships engaged
in coastal and international trade.

To a large and continually increasing extent, food preparation takes place in large households. These consist partly of households within which all meals are eaten, and partly of households where one or some meals are eaten each day. The first group includes health institutions, the armed forces, prisons, student hostels, etc. and ships. These households serve food to approx. 170,000 persons daily, and according to available estimates, serve some 100 million hot meals per year. Households where one or some of the daily meals are eaten include hotels, restaurants, cafeterias, canteens, and daycare centres for children. In this type of large household about 55 million warm meals were served in 1971.

In a report produced by the Chr. Michelsens Institute in 1975 it was estimated that the amount of food used to prepare meals in large kitchens comprised from 10 to 12% of our total food consumption.

There are no especially reliable sources providing information on the number of large households. Table 5 is based on various sources.

It should be noted that these figures are

based on estimates and taken from different years, and that the sources use different definitions to some extent.

6.3.2 Income

At a low income level a large part of the income must be used to cover food requirements. Previously a primary problem for a large part of the population in Norway was precisely to get enough food. In large parts of the world this is still the basic problem.

Surveys of consumer expenditure by the Central Bureau of Statistics provide information on how the consumption of goods and services has gradually changed in this country as economic well-being has increased. The last survey, which was made in 1973, showed that a steadily smaller proportion of the total household expenditure went to buy food. At the same time a steadily increasing share of the expenditure was used in other areas, such as tourism and transportation, leisure pursuits and education.

According to the consumer surveys of the Central Bureau of Statistics, the percentage

Table 6.

Annual expenditure on foods as a percentage of total consumer expenditure according to size of households in 1973.

	Total consumer expenditures per household (N. kr.)							
	under 10,000	10,000—14,999	15,000—19,999	20,000—29,999	30,000—44,999	45,000—59,999	60,000—79,999	80,000
Single persons	40.2	30.3	23.1	18.4	12.3 ¹⁾			
Couple without children	51.0	43.8	34.4	30.0	23.6	16.3	12.2 ²⁾	
Couple with one child under 16 years				31.2 ³⁾	24.7	21.6	15.6 ³⁾	
Couple with 2 children under 16 years				34.1 ³⁾	26.2	22.2	20.0	13.7
Couple with 3 or more children under 16 years				37.7 ³⁾	31.3	27.1	20.4	17.2

¹⁾ Includes households with incomes higher than 29,999.

²⁾ Includes households with incomes higher than 59,999.

³⁾ Includes households with incomes lower than 30,000.

Source: NOS: A705 (1975) Central Bureau of Statistics, Consumer Surveys, 1973.

expenditure on food for an average family has developed as follows:

1958: 39.9%

1967: 29.6%

1973: 24.0%

The decline can be registered for almost all types of foodstuffs.

Expenditure on food varies markedly, however, within the different households and income groups.

Proportionally, expenditure on food declines with rising total expenditure, from 43.2% for average households with a total consumption expenditure under 10,000 N. kr. to 15.7% for households with a total consumption expenditure of 80,000 N.kr. and over. The share spent on food rises with an increasing number of children and with increasing age of the primary wage-earner.

Table 6 provides some information on the proportion which expenditure on food comprises of the total consumption expenditure according to the size and consumption expenditure of the household.

The figures give some information regarding trends in total expenditure on food, but tell nothing about what lies behind these figures as regard changes in the consumption of different foods. Nor do they indicate anything about price trends.

The increase in income which has taken place in Norway has had a great influence on the type and amount of foods eaten. It is known that with higher incomes there is an increased consumption of eggs, meat, vegetables and fruits, cream and butter, while the consumption of cereal products and margarine falls.

Increased incomes have resulted in better and more varied diets, but also in too large a consumption of fats and sugar products, often at the expense of cereal products.

This implies that in the years ahead, unless active measures are employed, we cannot necessarily anticipate the achievement of a correct diet in accordance with the goals drawn up in this report.

This is also confirmed in the prognoses which have been made on the dietary pattern in the future, presented in Appendix 2 (not translated).

6.3.3 Knowledge and Skills

The household one lives in as a child will be the starting point for the experience, skills and knowledge acquired during life. Knowledge and skills will vary from household to household, depending on a number of circumstances.

Later on, skills and knowledge are acquired outside the household. An important element is the instruction everyone receives in elementary school.

A smaller part of each succeeding age group will also receive shorter or longer period of special education regarding knowledge and skills in the dietary field.

The majority will eventually take over direct responsibility for their own diet.

The knowledge and skills which are acquired outside the household one grows up in are mainly limited to those acquired as a result of education, information and marketing. Marketing measures are discussed in Section 6.2.4.

Education

The instruction which is given in the schools has three main purposes:

- to give all children an elementary knowledge of diet, especially about the relationship between diet and health, as well as providing the necessary skills,
- to give those who are directly responsible for the diet of others in various ways a more thorough introduction to the field and provide more skills than the elementary school can give, and
- to give a broader knowledge to those groups which will be responsible for teaching and guidance in the field.

Instruction aimed at providing knowledge and broader skills and at influencing the pupils' routines and attitudes takes place at different levels, according to age and the purpose of the type of school.

Nursery and elementary schools primarily shape attitudes. In the elementary school, the composition of food and the nutritional requirements for different groups and different ages are also taught.

High schools and other schools which fall within the tenth to twelfth school years teach nutrition for occupations inside and outside the home and provide a basic education for occupations which require such knowledge. Vocational training for kitchen jobs comes at this school level. Special mention must be made of the instruction in schools for home economics and of the home economics curricula and departments in technical schools for trade and industry.

Other schools based at high school level (12th year of education) provide training for kitchen managers, stewards, hotel and restaurant managers, social workers and teachers. Instruction in nutrition, diet, foodstuffs and food preparation has a central place in the training of home economics teachers and general teachers with home economics as a specialization. About 150 home economics teachers are trained each year.

Training at the academic level is given in the medical and odontology faculties and in the Nordic School for Nutrition at the University of Oslo.

The schools and types of schools described which provide instruction in nutrition or related subjects have either recently adopted revised teaching plans, are carrying out revisions, or will revise their curricula in the near future. In general, it seems that instruction in nutrition is for the moment well covered in the curricula, even though its extent varies somewhat. A general description is given in Appendix 5 (not translated).

Information

In Norway, the informational activity on diet has been carried out by a number of institutions and organizations, journals, weekly magazines and daily press, and on radio and television. So far there has been very little coordination of this work.

The public institution which has the responsibility for preparing expert guidelines for informational activity is the National Nutrition Council. Recommendations on the nutritional content of the diet were made by the National Nutrition Council in 1954 and were most recently revised in 1971. In addition to these, the National Nutrition Council has made recommendations on the amount and type of energy providing nutrients in the diet. (See Appendix 1, not translated).

The National Nutrition Council has also issued statements on nutrition aspects of curricula, teaching aids, etc.

Within the health sector, health clinics and school and public dental services play an important role in regard to information on nutrition.

The health clinics give guidance on nutrition for infants and small children and provide information about dental health.

Such guidance and information can be given during check-ups at the health stations, during home visits by public health nurses, and in courses for parents and parents to be. In this connection the Directorate of Health has produced pamphlets and other educational materials for use at the health stations, etc.

Considerable emphasis is also placed on information on diet and nutrition in the preventive dental health work which is carried out in the schools and within public dental services.

Experts at Norwegian universities have also given dietary information. This has primarily taken place in connection with matters of principle and has been directed toward special groups, though a certain amount of information has been aimed at the general public.

The public institution which reaches the largest number of people with its informational activities is the Norwegian National Broadcasting Corporation (NRK). Both radio and television carry programmes on diet and nutritional questions. Topics include information on food dishes, on the world situation in regard to food supplies, on dietary habits and health questions, about economic and environmental factors influencing the diet, on the durability of food when kept cool or frozen, etc.

Television sends 15—20 programmes or parts

of programmes annually in the form of food or consumer programmes. In addition there are reports on the newscasts. In the course of a year the radio will carry more reports than television because of the much longer broadcasting time.

Among other bodies which have been concerned with information, the Consumer Council and the State Institute for Consumer Research should be mentioned.

The Home Economics Advisory Service was combined with the Consumer Council in 1973 and is concerned with diet and food preparation, etc. Extensive course activity is carried out across the entire country. Through an expansion of the county offices of the Consumer Council there is now scope for much broader consumer guidance than previously. Information about nutrition, diet and food is also spread through the journal of the Consumer Council. The State Institute for Consumer Research produces material for use in teaching and information about diet and on the use and preparation of food, etc. The institute is continuing the activity which the former State Home Economics Information Office conducted from 1938.

The Committee for Informative Labelling and the Ministry of Consumer Affairs and Government Administration are responsible for the voluntary and compulsory labelling of consumer goods respectively. Special regulations for the compulsory labelling of pre-packaged foods have been approved and will come into effect on July 1, 1976.

Within the social sector health clinics give guidance to mothers on dietary matters. Guidance is also given to some extent through the school dentist.

Among the private organizations, the National Association for Nutrition and Health holds a unique position. It was established in 1955 on the initiative of researchers and medical doctors who worked in fields related to nutrition, after the matter had been discussed with the Directorate of Health and the National Nutrition Council. One goal was to provide guidance, advice and information on nutrition and diet. The main emphasis in this work has been placed on the preparation of educational and informational material and on information for professional groups which guide the public (dentists, health personnel, teachers), the preparation of correspondence courses, editing of manuscripts of textbooks, etc. As a basis for this activity, the Association on its own initiative carried out a series of dietary studies. Other nation-wide organizations which have been engaged in information work are the Norwegian National Health

Organization, the Norwegian Housewives Organization, and the Norwegian Co-operative Union and Wholesale Society.

The amount of information on dietary matters given by public institutions has been modest in comparison with product-directed information through commercial channels.

6.3.4 Dietary Pattern

The consumption of food in the household takes place in fixed ways. The dietary pattern is a set of more or less strict, unwritten rules which concern food consumption.

Essential principal elements in the dietary pattern are the choice of foods, size, frequency, timing and composition of meals and variation. Every dietary pattern is based on a limited number of basic food. Within this pattern there are a number of important commodities which comprise a significant part of the diet and which cannot be dispensed with without a break being felt in the dietary pattern.

Frequency and size are determined by physiological needs (the necessity of a more or less reasonable distribution of the energy supply throughout the day), and the time by practical circumstances (sleep, work, rest, etc.)

The two main types of meals in the Norwegian diet are somewhat differently structured. Bread meals consist primarily of open sandwiches (i.e. bread, butter and spread in a definite quantitative relationship) and a beverage. The typical dinner meal is a main course of meat or fish with boiled potatoes, and possibly vegetables, sauce, etc. There are also limits for the quantitative relationship here.

The nutritional composition of the meals can vary. The variations are considerably greater as regards hot meals than in the bread meals. This mainly concerns the choice of raw materials for the main course, which may be either meat or fish or different types of products within each of these groups.

The dietary pattern has consequences for the consumption of food and for the nutritional composition of the diet. It provides a framework for the proportion each separate group of products comprises in the diet. This is determined by the place the product has in the dietary pattern, i.e. which meal it belongs to and how often and in which amount it can be used.

The consumption of various foods is interrelated, because some foods are used as alternatives, others in combination. In the Norwegian diet, for example, meat and fish replace each other as main courses for dinner

within fairly wide limits. Within each of the groups there are many products which can be used as alternatives. In almost all instances, however, the main course is combined with potatoes.

Some of the nutritional consequences of the dietary pattern are that the energy supply is more or less reasonably distributed throughout the day and the individual meals have a tolerably balanced content of necessary nu-

trients.

The dietary pattern of a group is no guarantee of safe nutrition, nor that it is necessarily the most suitable. However, both nutritionally and practically, it represents a solution which has proved operative and carries certain advantages, and changes can lead to disadvantages. Attempts to deliberately change food consumption patterns demand considerable efforts.

Chapter 7. Goals of the Nutrition and Food Policy

7.1 INTRODUCTION

In the view of the Government, the nutrition and food policy should coordinate several important objectives and considerations. These may be summed up as follows:

1. Healthy dietary habits should be encouraged.
2. A nutrition and food policy should be formulated in accordance with the recommendations of the World Food Conference.
3. For reasons connected with the question of supply, the policy should aim at increased production and consumption of domestic food and at strengthening the ability to increase rapidly the degree of self-sufficiency in the food supply.
4. For regional policy reasons the highest priority should be placed on utilizing the food production resources in the economically weaker areas.

A primary task of the future nutrition and food policy will be to achieve an active co-ordination of these considerations. A good diet must be adequate, safe and suitable. It is necessary to have a diet which provides sufficient energy and which ensures adequate supplies of all necessary nutrients and other desirable ingredients. The diet which is offered must be safe in that it provides the basis for general good health and does not have any special harmful effects. The diet should be suitable, such that the prevailing dietary habits, the supply of foods, etc. are given the necessary consideration. Changes in the diet which are necessary for reasons of health are examined more closely in Section 7.2.

On the basis of the recommendations of the World Food Conference, it is proper to consider the nutrition and food supply policy in relation to the global production and supply situation.

As a step in solving the world food problem, it was recommended that the developed countries increase their food production as well as undertake measures to improve consumption patterns. However, such measures must take the trade policy interests of the developing countries as presented in international organizations, into consideration.

The Government attaches great importance to measures which can strengthen our future supply situation. Considerable attention must be paid to even a small likelihood of a supply shortage from abroad of such vitally necessary commodities as food. An increase in production will not be sufficient to ensure our food supplies.

It will be necessary to improve the supply situation in several areas concurrently, (1) through increases in the production and consumption of Norwegian foods, (2) through storage measures, (3) through a better organization of imports, including delivery agreements with other countries, and (4) by improving the capability to rapidly increase the degree of self-sufficiency. The effects of these measures must be evaluated in total, and the consequences they will have for other areas of the society assessed.

An increase in the production of food is a necessary prerequisite for covering a larger share of our food consumption through Norwegian production. The main points concerned in this will be examined in this report.

Storage measures make it possible to limit the effects of variations in crop levels and supply failures over a shorter period. The Government is working on plans for expanding the emergency stocks of food grains and feed concentrates.

Plans are also being developed for expanded emergency stocks of agricultural input commodities. These will be presented to the Storting as separate matters.

The organization of imports will influence the supply situation. Delivery agreements, especially with our neighbouring countries, can help to secure the supply situation.

Agreements on deliveries of grain to Norway from Finland, Sweden and the USA have been entered into. The agreements with Finland and Sweden are also examples of how the food supply situation may be seen in a Nordic context. The question of possibilities for Nordic cooperation in connection with food supply has been taken up in the Nordic Council.

The possibilities for rapidly changing consumption and production patterns in a crisis situation, so as to rapidly increase our degree of self-sufficiency will be of vital importance in evaluating our supply situation. These questions are being examined by a commission appointed by the Ministry of Trade and Commerce.

The Government attaches decisive importance to the contributions of the primary industries of agriculture and fishing in stabilizing settlement in economically weak areas.

The increase in agricultural production should therefore mainly occur in the economically weak areas.

These four important considerations in the formation of our nutrition and food supply policy must be balanced against each other.

The proposed policy involves the work of several ministries and concerns many industries, businesses and interest groups. This presupposes a considerable coordination of production and consumer policy. Changes in the diet must be made by individuals and in the individual households. It goes without saying that any change in consumption patterns will be a result of a voluntary change in dietary habits by the consumers. The Government's task is to stimulate a desirable dietary development through various measures.

The nutrition and food policy prepared by the Government will constitute an important national challenge which will involve the entire population. The proposed changes deviate from the prevailing development trends in countries with a high and increasing material consumption.

An increase in the production of agricultural products will require changes in our agricultural policy. It will mean the utilization of resources for agriculture which could otherwise be used by society for the production of other goods and services. The increase in the production of agricultural products must therefore take place at a pace which allows consideration of the need for increased resource input in other areas of society.

In this chapter the Government will examine the goals and guidelines of the nutrition and food policy in greater depth.

7.2 RELATIONSHIP BETWEEN NUTRITION AND HEALTH

An explanation is given in Chapter 2 of the most important development trends in the health situation in relation to changes which have occurred in our diet. The health situation has improved considerably since the turn of the century as measured by a number of criteria. This occurred during a period when the diet became richer and more balanced and the overwhelming majority of the population has become better supplied with the nutrients necessary for good health. An essential goal is to preserve the beneficial aspects of our present diet.

However, development trends in the health situation are not all positive. The expected lifespan for men over 50 has shown a decline. By far the greatest cause for anxiety is the increase in cardiovascular disease, but a high frequency of tooth decay, obesity and certain digestive diseases also gives cause for concern.

There must also be an awareness of the different nutritional requirements of special groups. There should be a special awareness of the growing tendency to obesity in children. To some extent elderly persons tend to

have an unbalanced diet with little variation and even malnutrition. This can result from a lack of information, or difficulties in shopping for, preparing and utilizing food.

Considerable shifts have taken place in the number and types of energy providing foods. The proportion of fats in the energy supply has increased, with saturated fats comprising a large part of the increase. The proportion of carbohydrates has decreased, with a reduced consumption of starches, although the consumption of sugar has increased.

The relationship between diet and health, such as that between diet and the cardiovascular diseases, is not completely known. Enough is understood about these relationships, however, to recommend changes in the diet which are desirable as a means of combatting these diseases.

As explained in Appendix 1 (not translated), the National Nutrition Council is responsible for making recommendations on the nutritional composition of the diet. These recommendations concern:

1. The supply of essential nutrients.

As mentioned, the diet of the population is largely satisfactory in this regard.

2. The amount and type of energy providing foodstuffs.

The recommendations conclude that fats should supply a maximum of 35% of the energy in the diet. Our diet does not correspond to the recommendations on this point in that more than 40% of the energy in the food supply come from fats. Dietary studies of the intake of individuals confirm that a high fat content in the diet is normal.

The National Nutrition Council stresses that a reduction of the energy supply from fat requires a corresponding increase in the energy supply from carbohydrates. There should be a greater use of starches. The consumption of sugar should be lowered rather than increased.

The National Nutrition Council further recommends that the proportion of polyunsaturated fats should be increased, bringing the ratio of polyunsaturated and saturated approximately 1 : 2. The present ratio is somewhere between 1 : 4 and 1 : 3.

An increase in the consumption of starch will primarily involve an increased consumption of cereal products. This, together with an increased consumption of potatoes, vegetables, fruits and other relatively energy poor foods, will be beneficial in several nutritional respects.

In the opinion of the Government, because of the adverse health tendencies mentioned earlier, especially regarding cardiovascular

diseases, and the insight we are gradually beginning to acquire about the relationship between nutrition and health, it is necessary to base the formulation of a nutrition and food supply policy on the recommendations made by the National Nutrition Council.

The Government will prepare a policy which will contribute to the following:

The beneficial aspects of the diet are to be preserved. Conditions will be arranged so that the diet is better adapted to nutritional requirements, while general demands for taste, variety and diversity are stressed. The different nutritional requirements of special groups such as children and young people, pregnant and breast-feeding mothers, the elderly, etc. must also be taken into consideration.

In order to obtain a better adaption of the diet to nutritional requirements it is especially important to curtail the proportion of fat in the energy supply. An objective should be to reduce the proportion of fat to 35% of the energy supply through a gradual alteration of the diet.

The decrease in the supply of fat should be replaced by foods containing starch — primarily cereals and potatoes. There should be an attempt to limit the proportion of sugar in the energy supply.

The proportion of polyunsaturated fatty acids in the total fat intake should be increased.

These objectives are based on present knowledge on what constitutes a safe diet, i.e. a diet which provides the basis for general good health and which does not have any special harmful effects. The Government assumes that knowledge of nutritional relationships will gradually expand both in extent and depth. It is felt, therefore, that it will be necessary to gradually adjust the goals as new knowledge is acquired.

The objective of meeting health requirements does not necessitate drawing up an 'ideal diet' containing definite amounts of various foods. The goal can be reached through different combinations and amounts of food. Solutions must be selected which are suitable in regard to the supply situation, resources, family economy, mode of living and other practical circumstances, and which at the same time satisfy reasonable demands for taste and variety, etc.

7.3 ADAPTION OF THE DIET

In Section 7.2 a number of the basic goals in the nutrition policy are discussed from the standpoint of health. Within this framework there is considerable scope as to which foods

and amounts can be included in the diet. This means that it is possible to take into account the other objectives in the nutrition and food policy summarized in Section 7.1.

It is indicated in Chapter 3 that there will probably be considerably greater uncertainty connected with the global supply of food in the next 10 to 15 years than there has been in the past. The Government feels this uncertainty and the recommendations by the World Food Conference should be met by increasing the production and consumption of Norwegian foods, at the same time changing the diet according to health considerations.

A balance between a reduction in the fat content in the diet and an increase in food production will be the most difficult to achieve.

In order to reduce fat consumption it is necessary to spotlight those foods which contain especially large amounts of fat.

Figures for the wholesale consumption of foods in kg per person per year in 1973 showed that 93% of the total fat content came from the food groups comprising margarine, other fats, whole milk, cream, cheese, butter and meat. Of these groups, margarine contributed the largest proportion, namely about 32% of the total consumption of fats.

It is a reduction of the fat intake from these foods which will count most towards reducing the fat content of the diet. The various sources of fat must be seen in relation to each other, so that the combined fat proportion is reduced to 35% of the energy content in the diet.

The production of milk plays an important role in our food production. Milk production provides nutritionally rich and valuable food products, of which a relatively high consumption should be maintained. The consumption of skimmed milk should be considerably increased as compared with whole milk, and the consumption of cream should be reduced.

Meat production is a necessary link in the utilization of our resources. The present development tendencies imply that consumption will increase considerably in the next 10 to 15 years. Even if meat does not contribute as largely to fat consumption as, for example, margarine and whole milk, a continued increase in meat consumption will hardly be expedient, considering the desire to reduce the intake of fats. On the basis of a total assessment, as objective should therefore be to hold the consumption of meat per person at about the present level. A reduction in the fat content in meat should be aimed at.

Considerations concerning Norwegian food production will however mean that only a

limited reduction of the fat consumption from milk and meat is possible. If the consumption of fats is to be brought down to a reasonable level from a health point of view, the consumption of margarine and of those types of fats listed in the statistics as «other fats» must be reduced considerably.

In the production and consumption of margarine and other fats, consideration must be taken of the wish to secure the sale of domestically produced hardened marine fats, while at the same time ensuring a satisfactory composition of fatty acids. An objective should be to increase the proportion of polyunsaturated fats in the diet.

The production of margarine and margarine products is based on hardened marine fats and vegetable fats. In recent years marine fats have comprised 45% of the raw material. The vegetable fats have been divided between approx. 30% vegetable oils, approx. 15% hardened vegetable fats and almost 10% coconut fat. Of these types of fats, vegetable oils have the most favourable composition of fatty acids, with a large proportion of polyunsaturated fats. Hardened marine fats, coconut fat and hardened vegetable fats mainly consist of saturated fat. The category «other fats» has gradually assumed an increased importance in the diet. There is incomplete knowledge of the areas of use and composition. The calculations which have been made indicate that the category «other fats» comprised 18% hardened marine fats and stock fat and 82% imported vegetable fats.

In the view of the Government, an attempt should be made to ensure the use of hardened marine fats in the margarine industry as far as is sound in regard to a favourable composition of fatty acids in the diet. It will be reasonable to use hardened marine fat instead of hardened vegetable fat in margarine production. The proportion of hardened marine fats could thereby be increased from 45% to 60% of the raw material in this production.

The diet must have a sufficiently high energy content. The decrease in fat content must be replaced, and it is most expedient that this be done by considerably increasing the consumption of cereals, as well as of potatoes and vegetables as compared with present consumption and that which is likely if present trends continue.

It will be correct to increase the consumption of fish and fish products considerably. The diet adjustments recommended on the basis of nutritional evaluations together with the proposed increase in food production will contribute to a more vegetable type of diet.

At the World Food Conference in Rome it

was recommended that the industrialized countries increase their food production and develop a coordinated nutrition and food policy. At the same time, however, it was pointed out that an important link in the solution of underdevelopment and food supply problems, was that the developing countries be assured access to the markets in the industrialized countries for all their products. The Government therefore feels that the way in which the consumption of domestically produced foods is increased will be significant. The natural conditions in Norway are not favourable for the production of agricultural products such as tropical fruits, cocoa, etc.

The import of grain should be reduced by increasing Norwegian grain production for food and animal feed and increasing the use of roughage at the expense of imported feed concentrates in livestock production. The large grain exporting countries are industrialized countries, while the developing countries are net importers. An increase in the consumption of domestically produced foods along these lines will therefore not be inconsistent with the interests of the developing countries as these are expressed in international fora.

7.4 INCREASING THE CONSUMPTION OF FISH AND FISH PRODUCTS

Norway is a substantial fishing nation, but only a limited part of our fishing catch is used directly for food. An increase in the direct use of fish as food will increase our consumption of foods of Norwegian production and contribute to a better exploitation of resources. Fish has a relatively low fat content and a favourable fat composition.

In the view of the Government a substantial increase in the consumption of fish per person should be an objective during the next 10 to 15 years. If such a goal is to be reached, however, it is necessary to present a greater choice of food products based on fish or with fish as one of the ingredients. It is therefore important to put emphasis on research related to raw materials and product development.

Considering the limitations which the fishery resources themselves impose on Norwegian fishing, it is important to develop products and production methods which can result in a larger part of the total Norwegian catch being utilized directly for human consumption.

The Government feels an objective should be to ensure the use of hardened marine fats in the margarine industry as far as is reason-

able with regard to a favourable fatty acid composition in the diet.

In Appendix 6 (not translated), prepared by the Budget Committee for Agriculture, an example is given of a diet which corresponds with the assumptions on which this report is based. (See Table 7.) An increase in fish consumption from 28 to 40 kg per person is estimated during the period up to 1990. In order to reduce the proportion of fat in the diet, a fall in the consumption of margarine from 19 kg in 1973 to 12.5 kg per person in 1990 is assumed. The proportion of hardened marine fats can be increased, however, from approx. 45% to 60%.

The consumption of fats in the category «other fats» (calculated as 100% fat) is assumed to fall from 6 kg per person today to 4.2 kg per person in 1990. A constant proportional distribution of «other fats» is assumed for the entire period. Thus the proportion of total food supplied by fish and fish products will therefore be 7.5% both in 1973 and 1990. The consumption of hardened marine fats on the Norwegian market will be maintained because of the increase in population and in 1990 will be in line with the 1973 level.

7.5 INCREASE IN AGRICULTURAL PRODUCTION

In Report No. 50 for 1974—75 to the Storting on Natural Resources and Economic Development, the Government has evaluated the considerations which must be stressed in assessing the size of agricultural production in our country. These can be summed up as follows:

1. Consideration of the future supply situation implies an increase in agricultural production.
2. An increase in agricultural production can contribute to the stabilization of settlement in economically weak areas.
3. Increases in agricultural production should occur in such a way and at such a pace that satisfactory consideration can be taken of increased efforts in other areas of society.

In the above-mentioned report (Stortingsmelding No. 50 for 1974/75), it is pointed out that a definite degree of self-sufficiency in certain commodities can never be a goal in itself.

How much emphasis is to be accorded to preparation to meet emergency situations in the various commodity and industry groups must be decided on the basis of evaluating the possibilities of an increased scarcity. For most raw materials and finished goods, the risk of

supply failures in the short and medium term are considered to be small.

However, for certain vitally necessary commodities such as foods great significance must be attached to even a small possibility of a failure in supplies from abroad. Therefore emergency considerations have always played a role in justifying economic and other measures to strengthen agriculture.

Agriculture plays a basic role in the income of and settlement in many economically weak areas. The development in agriculture and agricultural production in these areas will have great significance for regional policy. Production resources in agriculture should therefore be exploited so that farming — together with other industries — provides the basis for an effective regional policy.

In Report No. 50 for 1974—75 to the Storting on Natural Resources and Economic Development it is stated that a basic question in the years ahead will be how we as a nation should utilize our resources for the production of various goods and services. In assessing employment, emphasis must be placed on the danger of substantial readjustment problems in industry. An increase in agricultural production assumes therefore that resources will be employed in this sector which could have been used in the production of other goods and services for the society. An objective should be a development in agricultural production which also takes into reasonable consideration the need for increased efforts in other areas of society.

In the above-mentioned report, the Government has made a total evaluation of the considerations which should be basic in assessing an increase in agricultural production. The Government has concluded, mainly because of settlement structure consideration and the desire to reduce readjustments, but also because of the uncertain conditions in the world food market, that a greater production of agricultural products should be aimed at in Norway. In this section these questions will be examined more closely.

A standpoint will be taken on some of the questions discussed in the report by the Committee for Evaluating Support Arrangements for Agriculture (The Øksnes Committee). The production goal for Norwegian agriculture, and central issues in farming objectives in relation to regional policy will be discussed. The other goals for farming policy and the measures which should be implemented to reach these goals will be discussed in more detail in a report to the Storting on farming policy.

In this section the main trends in the development of Norwegian agriculture up to

1990 are outlined. The Government, however, has not discussed nor taken any stand on an overall plan for the development up to 1990. This will be taken up in the usual way in long-term programmes, and annual and long-term budgets, and the Government and Parliament will of course return to these questions in such contexts. The uncertainty which is always connected with planning over such a long period of time should be noted.

On the basis of the present production goals, the task for agriculture should be to cover the national requirements for milk and milk products, cheese, butter, meat, potatoes, eggs, and as much vegetables, fruits and berries as possible. For these products, production should be adjusted in relation to consumption, and an attempt should be made to keep consumption in accordance with the recommendations based on supply and nutrition considerations. A substantial increase should be aimed at in the production of grain. A large part of this increase should comprise food grain. There is also a need for increased berry production. The production of sugar in Norway is not of current interest.

In Chapter 5 it is shown that a substantial increase in the agricultural area is possible. However, possibilities for increasing the grain area through new cultivation are limited. The interesting question will be how far and how rapidly these resources should be put to use within the framework of the production goals.

Both for general reasons and with regard to the farming industry, a gradual and long-term increase in production should be aimed at. On the basis of a total evaluation of the considerations which must be weighed against each other, the Government has decided that the agricultural area in use should be increased from 9.0 million decares in 1974 to 10.0 million decares in 1990.

The fully cultivated area should be increased from 7.9 million decares in 1974 to 9.0 million decares in 1990. Regional policy considerations call for the main weight of the net production increase to occur in the economically weak areas. In 1971 55% of the agricultural area was in economically weak areas.

An objective should be that at least $\frac{3}{4}$ of the net area increase up to 1990 should be in economically weak areas.

Area requirements for potatoes, vegetables, fruits and berries are related to the level of consumption and crop yields. It will not be necessary to increase the area for these crops to any degree.

The production of roughage should be increased to somewhat above the present

level. An increased production of roughage at the expense of feed concentrates in milk production is aimed at, and a limitation of the use of feed concentrates in meat production.

The production of grain plays a central role in our food supply. In 1975 the grain area was 3.0 million decares. The main part of the production was used for fodder. The grain area should be increased to 3.6 million decares by 1990. A substantial part of the increased grain production should comprise food grains, so that food grain production in normal crop years reaches 125,000 tons (350—400,000 decares). The major food grain will be wheat, but the consumption of other types of grain for food should be stimulated.

The planned increase in agricultural production deviates from the development trends we have had in recent years. In the period 1969—74 employment in agriculture was reduced by 8,200 man years annually, or about 40,000 man years in all. The number of farms was reduced by 6,800 per year, or 35,000 farms in all, and the agricultural area in operation reduced from 9.9 to 9.0 million decares. In the last two to three years these development trends have slowed considerably. It must be expected, however, that the first and most important task will be to change the lines of development so that the decrease in agricultural areas in operation is halted, thus limiting the decline in employment in agriculture. It must be an objective to gradually increase the agricultural area. A limited increase will be realistic up to 1980. The main part of the increase should occur between 1980 and 1990.

The increase in the production of agricultural goods will have consequences for the use of more manpower and the need for investment in farming. The Government has decided that the increase in agricultural production must be based on the evaluations in Report No. 50 for 1974/75 to the Storting. The Secretariat of the Budget Committee for Agriculture has made calculations for the development in manpower up to 1990. (Appendix 6, not translated). These calculations show a rise of 3,300 man years per year in the period 1974—80 and of 900 man years per year in the period 1980—90.

The reduction in the number of farms is estimated at 3,100 in the period 1974—80 and at 800 per year in the period 1980—90. These calculations are based on the size of production and probable estimates of the use of labour input per unit produced.

According to the Government's evaluations there is little doubt regarding a rapid development of effectiveness in agriculture in the

central areas. A continued rapid development of productivity should be especially stimulated in the production of plant products for sale (grain, potatoes and vegetables). An increase in grain production in the central areas will provide the basis for a continued rapid development of productivity.

The Government has planned a better exploitation of agricultural resources other than farming. This applies primarily to lumbering (See Report No. 110 for 1974—75 to the Storting), but also to the other agricultural industries. A development in this direction will contribute to a better exploitation of manpower on farms without any negative effects on agricultural production.

In the years ahead the Government will strengthen measures in regional policy aimed at a better regional distribution of employment. For many farms this will imply a substantial improvement in labour opportunities outside the farm, while at the same time enabling agricultural production to be maintained or increased.

On the basis of a total assessment the Government has decided that the assumed increase in agricultural production in the period 1974—80 is possible with a decline in employment of 21—24,000 man years (3,500 to 4,000 man years per year). In the employment estimates in Report No. 50 for 1974—75 to the Storting a decline of 27,000 man years for the period 1974—80 was used as a base. Even if a lesser man power decrease in agriculture is aimed at, there is such great uncertainty connected with the employment estimates, both in general and as related to the various branches of agriculture industry up to 1980, that this adjustment does not necessitate a total reassessment of the figures in Report No. 50 to the Storting.

The 1970 census showed that 33,000 or 25% of the 131,000 employed in agriculture were over 60 years of age. This means that age alone will contribute to a large decline in the numbers employed in the 1970's.

When considering developments in production and the formulation of farm policy measures, priority should be given to measures which will ensure that the actual decline in employment and the number of farms in the economically weak areas is considerably lower than that indicated by average figures for the country as a whole.

The Government will closely follow the development in employment and production in agriculture and return to these questions in the long-term programme for 1978—81.

An expansion of the agricultural area from 9.0 to 10.0 million decares and an increase in

the fully cultivated area from 7.9 to 9.0 million decares will entail that new cultivation is held at a relatively high level. It is stated in Appendix 3 (not translated) that the annual new cultivation in recent years has been 60—80,000 decares. In the last two years new cultivation has been over 80,000 decares. The loss of arable land for building development purposes was reduced to 11,000 decares in 1974.

The reduction of the agricultural area in recent years is primarily due to land going out of production through the closing of farms. A substantial part of this land is probably economically workable. The Government will apply the new land law regulation on failure to work arable land, so that interested farmers can bring economically workable areas into production.

On this basis of a total evaluation the Government has decided that new cultivation on an average of 80,000 decares per year will be adequate in the next 10 to 15 years. Most of the new cultivation (about $\frac{3}{4}$) should occur in the economically weak areas. This will be necessary to strengthen farming in these areas. The new cultivation in the central areas will take place substantially in highly productive forests which also function as recreational areas. With regard to future lumber production, an attempt will be made to limit new cultivation in such areas. However, it will be important to increase efforts to level off steep agricultural areas in the central districts.

The need for investment in agriculture is a central question.

In Report No. 50 for 1974/75 to the Storting on Natural Resources and Economic Development it is estimated that the gross investments in agriculture will increase by 1.4% per year in the period 1974 to 1980. A considerably greater growth is now anticipated.

The calculation made by the Budget Committee for Agriculture shows that gross investments in agriculture must increase from 1,667 million N. kr. in 1975 to 1,862 million N. kr. in 1980, measured in 1974 prices (2.2% annual increase). The increase from 1980 to 1990 is estimated at approx. 0.8% per year, about half going to farm buildings.

In order to ease the financing of agricultural investments the Government Bank of Agriculture raised credit limits for agricultural purposes to 240 million N. kr. in 1975, as against 199 million N. kr. in 1974.

The limits are set at 280 million N. kr. for 1976.

The Secretariat of the Budget Committee for Agriculture has estimated the effect that

the presumed conditions are likely to have on the degree of self-sufficiency.

With the planned expansion of agricultural production, the estimates of the Budget Committee for Agriculture indicate that the proportion of the food energy supply from Norwegian agricultural products will increase from 40% in 1973 to almost 49% in 1990. The increase in the production of food grains and potatoes is the most important reason for this. According to calculations, Norwegian food grains will cover 28% of the consumption in 1990, while the Norwegian share in 1973 was 3%. Fodder grain production will increase and the consumption of feed concentrates will remain about constant. The import of feed concentrates according to these calculations, will be reduced from 782 million kg in 1973 to 423 million kg in 1990. The proportion of Norwegian agricultural goods produced with domestic land resources will thereby increase from just under 32% in 1973 to more than 44% in 1990.

7.6 COVERING FOOD REQUIREMENTS

The coverage of food requirements is illustrated by the degree of self-sufficiency. This provides an approximate expression of the domestically produced proportion of food requirements calculated on an energy basis. In addition, it is usual to correct the degree of self-sufficiency for the effect of the import of feed concentrates for agriculture. In this way we obtain an expression of the proportion of Norwegian produced agricultural products which are based on Norwegian fodder.

The degree of self-sufficiency provides no information, however, on the fact that food production is partially based on imported input factors such as machines, fuel, chemical fertilizers, etc., that fish, domestic animal products, marine oils, and herring and other fish meal are exported, and that production and consumption adjustments are possible in a crisis situation.

In Appendix 6 (not translated), prepared by the Secretariat of the Budget Committee for Agriculture, the development in the degree of self-sufficiency up to 1990 is calculated according to the basic assumptions in this report.

The degree of self-sufficiency, which has shown a slight tendency to decline in recent years, will increase according to these calculations from barely 48% at present to 56% by 1990. The increase in the degree of self-sufficiency will be a result of increases in the production and consumption of agricultural products from 40% of the food energy supply in 1973 to over 48% in 1990. This will re-

sult primarily from an increased production of food grains and potatoes. The consumption of fish and fish products (including marine fats) will remain constant at 7.5% of the energy consumption. This is because the increased consumption of fish will be balanced by a decline in the use of marine fats in the margarine industry. Because of the population increase the total consumption of marine fats on the Norwegian market in 1990 will be in line with that in 1973.

The degree of self-sufficiency corrected for the import of feed concentrates will increase from 39% in 1973 to 52% in 1990 according to the calculations. The corrected degree of self-sufficiency rises by 4.5 percentage units more than the uncorrected. This can be regarded as an approximate measurement of the effect of the assumed increase in domestic fodder production.

The Budget Committee for Agriculture estimates that the export of foods and fodder materials corresponds to 13.5% of the food energy consumption of the Norwegian population in 1973.

In addition there is the export of marine oils. The total quantity exported, if used directly for human consumption, would correspond to 25% of the energy consumption by the Norwegian population (See Appendix 6).

In an assessment of Norway's resource situation in a global context (NOU 1974: 55) it is estimated that the degree of self-sufficiency corrected for the import of feed concentrates can reach 55% in Norway. On the basis of the assumptions on which the Government has based the nutrition and food policy, this level would be approached by 1990.

The Norwegian import of foodstuffs will be concentrated on sugar (99% of total requirements) food grains (72%), fats for margarine (40%), other fats (80%), fruits and berries (65%), vegetables (15%) and fish. The proportion of fish consumption covered by import is estimated at 18% for 1974. The actual import is probably considerably lower since a large part of the import consists of fresh fish which is re-exported as processed products. However, there is no definite statistical information on this.

The main part of the fish production will continue to be exported, but the share which is used in Norway will increase somewhat. The proportion of the fish production which is utilized directly for human consumption will increase. Furthermore, a limited regulating export of milk products will be necessary, and periodically there will be a limited surplus or deficit of other commodities.

Our emergency food supply, with the re-

serves outlined, will be strengthened far more than the increase in the nominal degree of self-sufficiency indicates. This is related to the fact that, according to the assumptions, our import of feed concentrates will be greatly reduced. In a crisis situation it will be possible to increase the production of food grains considerably from one year to the next. We can also use more barley and oats for food by blending them in bread flour (20–30%) or in

other ways. This will entail a certain reduction in livestock production. It would also be acceptable on a temporary basis to replace most of the vegetable fats in margarine with hardened marine fats.

The Government is working on plans to expand the emergency stocks of food grains and feed concentrates. Reports are being prepared on expanded emergency stores of input materials for farming.

Table 7.

Norwegian produced share of total food consumption calculated on an energy basis.

	Registered figures		Estimates		
	Norwegian produced share				
	1973	1974	1990		
			Norwegian produced share	Total calories in 1000 mill.	Norwegian produced calories in 1000 mill.
Grain (as flour)	2,8	6,6	28	1 337	371
Food potatoes and potato flour	99,6	100,0	100	312	312
Sugar, syrup and honey	0,7	0,9	1	577	6
Peas, nuts, cocoa	—	—	—	113	—
Vegetables	85,9	81,7	87	39	34
Fruits and berries	26,7	37,9	35	153	54
Meat, excluding pork	91,5	93,4	100	163	163
Pork	95,6	91,1	100	235	235
Offals	100,0	100,0	100	19	19
Eggs	96,5	100,0	100	60	60
Fish	87,0	82,6	85	105	89
Whole milk	100,0	100,0	100	395	395
Cream	100,0	100,0	100	87	87
Skimmed milk	100,0	100,0	100	89	89
Condensed milk	93,7	93,5	94	67	63
Powdered milk					
Cheese	98,7	98,7	100	171	171
Butter	100,0	100,0	100	206	206
Margarine	41,9	48,8	60	398	238
Other fats	18,2	17,4	20	160	32
1. Total Norwegian produced share	47,7	50,8	56,0	14 686	2 624
2. Share of Norwegian produced agricultural products	40,2	42,5	48,5		2 275
3. Share of Norwegian produced fish and fish products	7,5	8,3	7,5		
4. Share of Norwegian produced agricultural products corrected for imported feed concentrates	31,7	34,5	44,4		2 001
5. Share of Norwegian produced food corrected for imported feed concentrates	39,2	42,8	51,9		

Source: Table 17 in Appendix 7 elaborated by the Budget Committee for Agriculture.

Report No. 32 to the Storting
On Norwegian Nutrition and Food Policy

Chapter 8. Measures for Implementing the Nutrition and Food Policy

8.1 INTRODUCTION

In Chapter 7 the Government has drawn up the long-term objectives of a coordinated nutrition and food policy. Decisive emphasis is placed on achieving a diet which is as favourable as possible from the standpoint of health, while at the same time creating greater security for the food supply than exists today.

In this chapter the Government will outline measures which must be implemented in order to eventually achieve a diet which corresponds as closely as possible to the proposed objectives.

A coordinated nutrition and food policy will strongly affect the area of industrial policy, and especially agricultural and fishery policies. Special measures in industrial policy will not be discussed in this report.

The following will therefore be limited to evaluating measures to promote a desirable diet.

A central and decisive point in planning a purposeful nutrition and food policy will be the institutional possibilities for following up such a policy. Extensive coordination between the different public bodies which work in fields affecting this policy will be necessary. The Government has outlined in Chapter 9 the institutional set-up which will ensure a follow-up of the nutrition and food policy. The various measures set forth in the following must be closely assessed in relation to the proposal for administrative follow-up outlined in Chapter 9.

The implementation of a nutrition and food policy requires cooperation between:

- the public sector
- trade organizations, firms and the active labour force, and voluntary organizations
- the various household groups.

The objectives should be realised in close cooperation with those who are and will be connected with the work on this policy.

The broad and objective interest which already exists in various groups of households, as well as the work which is already underway for providing increased knowledge and improved skills in this area, must be further expanded.

The diet of a country is the result of a large number of factors, as described in previous chapters. The nutrition and food policy ranges widely in that it will have an influence on many areas of our society:

- our import of foodstuffs
- production and processing
- distribution

- marketing
- the demand for foodstuffs, in which price, knowledge and skills, and dietary patterns are important elements.

An account is given in Chapter 6 of a number of factors which influence the consumption of foodstuffs. As indicated in this chapter, there is a set of factors which influences consumption. The total result of these effects can be illustrated above all by comparing the objectives in Chapter 7 with the trends which are found in Norway today. A number of these development trends must be changed if the goals are to be reached within a reasonable period of time.

Even though the nutrition and food policy covers a broad area, the effect on each field will often be relatively small. Of vital importance to the implementation of a national nutrition and food policy will be the degree of stability and effective coordination with which the work is carried out. In Chapter 9 of this report plans as to how work is to proceed in order to ensure the implementation of such a stable and coordinated policy are described.

An effective nutrition and food policy must be based on a total evaluation of all the measures, such that the various measures can be planned and implemented where they are appropriate and are found expedient. Certain measures must be considered as exerting a greater effect than others. Some measures may have relatively rapid effects, while others are primarily directed towards gradual and more long-term changes.

For the sake of perspective, measures can be divided into the following groups:

- Agricultural and fishery policy measures
- Price policy and consumer subsidies
- Measures concerning industrial processing and imports
- Measures concerning sales and marketing
- Information and education
- Regulations on the content and composition of foodstuffs
- Research.

Our nutrition and food policy must be largely based on the exploitation of Norwegian production resources. In earlier sections frameworks have been outlined for further development based on nutritional objectives, which take into consideration a good utilization of Norwegian production resources. Such changes may result in certain readjustment problems for firms and groups of employees. These problems will be given special attention.

In connection with the goals regarding adaption of the diet on which this report is based, the Government has made proposals which it will be realistic to fulfill in the course of a 10 to 15 year period. In the assessment, considerations has been given to what is a realistic goal as regards the changes in the production pattern which are felt reasonable and possible. Consideration has also been given to changes in the diet which are felt to be feasible in relation to measures which are realistic to employ. The basis of this policy is the goal of healthy nutrition.

8.2 AGRICULTURAL, FISHERY AND PRICE POLICIES

In the view of the Government, the formulation of consumer subsidies and agricultural and fishery policy measures should be assessed in relation to each other. These measures are very important to consumer prices. They should be evaluated together because, within certain areas, they supplement each other.

8.2.1 Agricultural Policy Measures

The agricultural policy measures are mainly formulated within the framework of the Agricultural Agreement (between State and farm organizations). The Norwegian market for important agricultural commodities is protected in various ways from competitive foreign imports. Within this framework, commodity prices are fixed and agreements are made concerning various special subsidies for production. The foodstuffs included in this system are milk and milk products, most types of meats, eggs, potatoes and non-perishable vegetables. Free imports of most perishable vegetables and fruits and berries are allowed part of the year. There is a clear relationship between the producer price and the consumer price for all agricultural products with the exception of milk products and grain. Prices for milk and milk products are not included in this context, since butter and cheese give a lower return for the raw material, while whole milk and cream give a high return. It is the Government's view that agricultural policy measures should be utilized in such a way that they are also nutritionally justifiable.

The question of to what degree it is possible to influence the nutrient content of agricultural products in desired directions through various measures is important in planning a nutrition and food policy.

Agricultural production takes place under relatively controlled conditions. The nutrient content of the products can therefore be influenced to a limited extent through plant

breeding and animal feeding and breeding measures.

Altering the ratio between fats and other nutrients in foodstuffs is of great interest from a nutritional point of view. This applies mostly to livestock products, due to both the fat content and the composition of fatty acids.

Price fixing vis-a-vis producers of individual livestock products stimulates the production of low fat content products. A price grading system is used in meat production which offers the highest prices to producers of good, meaty animals with a low proportion of fat. In milk production, the producer price increases with an increasing percentage of fat in the milk, but on the whole the price increase is lower than the production costs entailed in increasing the percentage of fat.

The National Association of Norwegian Milk Producers has plans to change the price calculation system for milk, so that milk price is based on the protein content. This will mean that any possible incentive to produce milk with a maximum fat content should disappear. The Government expects these plans to be implemented.

This is felt to be a good starting point for influencing the nutrient content in the desired direction. It is important, in the view of the Government, to carry this work further, and it is therefore believed appropriate to cooperate with the organizations in the milk and meat sectors on these questions.

There is a very strong hereditary relationship between the solids-not-fat content in milk and the percentage of fat. This means that it is difficult to lower the percentage of fat without at the same time reducing the content of proteins and other nutrients. Over a period, however, there seem to be certain limited possibilities for changing the ratio between fat and other nutrients in milk through breeding measures. Because of the central importance of milk in our diet, it should be an objective to strengthen research activity aiming at developing a breed of cattle which produces milk with a lower proportion of nutrients such as fat. It must again be stressed, however, that it is a very difficult and long-term task to change the ratio between proteins and fat in milk.

8.2.2 Fishery Policy Measures

The price of fish and fish products in Norway is influenced to a considerable degree by the world market price, as 85-90% of the production is exported.

This means that fishery policy measures such as are implemented under the Fisheries

Agreement (between State and fishery organizations) can not influence the domestic price level for Fish to any great degree.

The arrangement of compensation for value-added-tax was extended on August 15, 1975 to include fresh fish, herring and whale meat from Norwegian catches. The implementation of this arrangement caused a number of problems connected with the sales/distribution system for fish.

The Government intends to thoroughly assess the domestic sale of fish as soon as possible in order to bring distribution and sales into a rational and organized form, with a satisfactory control of profit and prices. The fact that this will probably result in increased consumption of fish will also make it easier for the authorities to implement various measures.

8.2.3 Price Determination

In Chapter 6 and Appendix 4 (not translated) the trade obligations Norway has assumed in regard to different types of foods are discussed. These obligations will have implications for the possibilities which exist to fix the prices of foods more or less independent of world market prices.

Due to different import restrictions for the various commodities, the price of certain foods is determined especially for the Norwegian market, while the price of other products is influenced to a greater or lesser degree by world market prices. Foods which are influenced by world market prices are sugar, margarine, vegetable oils and fats, fish and fish products, and some vegetables, fruits and berries. Food grains are in a middle position, as the State Grain Corporation is the sole importer, and special price and subsidy arrangements are formulated for food flour.

Even for commodities for which trade agreements allow the establishment of a price level independent of the world market price, practical possibilities are limited. With the increased contact between countries, an imbalance of trade could occur if price levels vary much from one country to another. In the case of Norway this means that in setting domestic prices, an eye must be kept on the price of the same products in our neighbouring countries. A current example of this is the price of sugar.

Traditionally, the prices of foods on the world market have fluctuated greatly. In recent years, these fluctuations have been especially large. Norway has supported proposals, in international organizations, intended to stabilize the prices of foods and raise these prices in relation to the prices of other pro-

ducts. A stronger degree of stability in world market prices for foods will make it easier to plan and carry out measures to achieve the specific aims of a nutrition and food policy. In this connection Norway has given approval to proposals on international commodity agreements. The work on establishing such arrangements is being carried out through GATT and UNCTAD, and these endeavours will be supported by Norway.

8.2.4 Use of Consumer Subsidies

For most subsidised commodities, subsidies are made up of compensation for value-added-tax consumer subsidies.

For the purpose of this report, compensation for value-added-tax and consumer subsidies are treated as one and designated consumer subsidies.

Consumer subsidies are important factors in general economic policy. The primary objective of these measures is to reduce the rise in prices. An important basis is that subsidies are applied to such commodities as will reasonably ensure that they will benefit the consumer and where arrangements can be implemented with reasonable administration and control. This limits the number of products which it is technically possible to include in this arrangement. Today there are consumer subsidies on milk, cheese, most types of meat, butter, margarine, fish, herring and whale meat from Norwegian catches, and food flour. Another objective is to apply subsidies in such a way that they especially benefit families with children and families with low incomes. It is also intended that they be utilized as a flexible measure in more short-term economic policy, where it might be of interest to both increase and reduce amounts over a short period.

Price policy considerations must in the Government's view, continue to be an important basic factor in subsidy policy.

In Chapter 6 there is a more detailed examination of the possibilities which exist to influence the demand for foods through prices. It is pointed out that the demand for foods such as milk, cereals and potatoes varies little with price changes, while there is a tendency for demand for cereals and potatoes to decline rather than increase with increased income.

Meat, including pork, is an example of a type of product where both changes in prices and income play a somewhat greater role as regards demand. As far as these commodities are concerned, the reciprocal price relation between meat other than pork and pork, and probably also the price relation between meat

and fish, are just as important as absolute prices.

It is considered that prices have a relatively large influence on the demand for products such as the more exclusive vegetables.

If prices are to be used to influence consumption, the greatest effect will generally be obtained by changing the relative price relationship between foods which satisfy the same requirements. Possibilities for influencing consumption through prices will also be related to a certain degree to income conditions in the society.

In the view of the Government, an objective in formulating subsidies should also be to influence the consumption of foods in the desired nutritional direction. The Government feels it will be possible to combine this goal with the desired aims for the use of subsidies in price policy.

8.2.5 Formulation of Price Measures for Individual Products

Price measures through the formulation of consumer subsidies, together with measures introduced as part of agriculture and fishery policies, will be necessary steps in a coordinated nutrition and food policy. It is not possible to put forward detailed proposals concerning the various measures. A constant follow-up will be necessary where the measures and changes in the dietary pattern are studied in relation to each other. However, the Government feels it is necessary to draw up certain principle guidelines for the use of these measures.

Grain. Cereals (food flour) should be relatively cheap and stable in price. Today we have a price system for grain where the price of cereals is independent of fluctuations in the world market price. This is achieved through variable subsidies. The price of food flour should be independent of the producer price for Norwegian food grains.

Potatoes. With the present sales system for potatoes, the use of subsidies has so far not been relevant. Possible consumer subsidies to stimulate the consumption of potatoes and measures in agricultural policy not dependent on prices should be assessed together.

Vegetables, Fruits and Berries. The use of consumer subsidies is not appropriate with the present sales system for vegetables. In order to maintain prices at a moderate level in order to stimulate the consumption of vegetables measures such as packaging subsidies, producer subsidies based on the area under cultivation, etc. should be introduced to indirectly reduce the price of Norwegian vegetables.

Under the existing sales system for fruits and berries subsidies are not appropriate. Considering trends in consumption, it is felt that measures other than price are of no real current interest for Norwegian goods.

The consumer prices for vegetables, fruits and berries vary greatly in different parts of the country. There are freight subsidies for citrus fruits and Norwegian apples and pears to North Norway (7.5 million N. kr. in 1975). These freight subsidies should be maintained and a wider application considered.

Sugar. Under the prevailing international commodity agreements which Norway supports, a stable price at a relatively high level must be expected. This could also contribute in preventing the consumption of sugar from becoming too high.

Meat. Meat consumption should not increase above the prevailing level. Meat subsidies should be formulated so that the consumption of meat per inhabitant, also in relation to fish, does not increase. This will limit the extent to which meat can be subsidized. As a part of the efforts to increase the degree of self-sufficiency, meat subsidies should continue to be formulated so that the consumption of «dark» meat (beef and mutton) is stimulated.

Whole Milk and Skimmed Milk. The fixing of prices under the Agricultural Agreement and subsidies should be examined in relation to each other, and formulated so that the consumption of skimmed milk is stimulated as compared with whole milk. There is a low price elasticity for milk, i.e. the number of liters purchased will vary very little with price fluctuations. On the other hand consumption could be shifted somewhat from one milk product to another by changing their price differentials. It is therefore completely reasonable from the point of view of the nutrition and food policy both to increase and reduce the rate of subsidies for these products. Partly skimmed milk should also be introduced on the market to give consumers a better and more varied choice of milks with a low fat content.

Cream. The fixation of prices under the Agricultural Agreement should be formulated so that consumption is not stimulated.

8.3 Industrial Processing

The industrial processing of food is discussed in more detail in Chapter 5.

Today most food is industrially processed to some extent. This has made it possible to satisfy the need for a larger selection and for larger amounts of foods.

The centralization of food production has made it easier to standardize the quality of foods and establish more effective food control.

This development should have offered possibilities for influencing the eating habits and diet of the population in a way favourable to health, but this has only occurred to a small degree.

It is assumed that the consumption of completely prepared dishes and meals will increase in the years ahead. This will contribute to increase the importance of industrially processed foods in a nutritional context.

In order to carry out the objectives of the nutrition and food policy it is necessary to have the active cooperation of the food industry.

The food industry will play an important role in regard to providing the population with a varied and suitable choice of foods in accordance with the objectives of the nutrition and food policy.

In this connection the Government will seek a close cooperation with the food industry organizations.

8.4 Distribution and Marketing

The formulation of distribution and marketing policies is based on the raw materials and the processing methods which are available. Sales activity must be regarded as a consequence of these two underlying conditions. This will usually mean that changed production conditions will be of direct significance for sales and marketing. It also means that measures which are aimed in isolation at influencing sales and marketing will sometimes be less effective than if more coordinated procedures were chosen.

Unfortunately, present marketing practices are in relatively large disaccord with the nutritional objectives. This disaccord, if allowed to operate in the same direction over a long period of time, may have consequences which limit the effectiveness of the nutrition and food policy to be followed.

The factors which today regulate sales are to only a small degree dictated by nutritional considerations. The measures serve other important purposes but often have unintentional consequences for the diet. In the longer run it must be an objective to formulate the distribution policy so that consumers can be assured a more suitable choice of foods presented in an acceptable way.

Public measures directly and indirectly influence sales and distribution. These can be formulated in various ways so that the diet is taken into consideration:

— In Appendix 1 to the budget proposals for 1975—76 the Ministry of Trade and Commerce (St.prp. Nr. 1) has presented proposals on two different subsidy arrangements to enable shops to maintain general store services in outlying areas. There is an investment support arrangement and an operational support arrangement. It is a condition for both of these that the shop must carry an assortment which covers the essential general store needs of the local population and makes possible a diet which is in accordance with the nutritional goals.

Health regulations for the sale of food must be examined in a broader context than has been the case so far. In working out such regulations, care must be taken in practice they do not lead to a reduced choice of suitable food products. This should be seen in connection with the trade firms being enabled better to fulfill such regulations.

A number of products which are mainly sold in kiosks and street kitchens, etc. have a less advantageous nutritional composition. In this area, the task is partly to ensure a better nutritional composition of those products now sold, and partly to see that more suitable products receive an increased share of the turnover.

Other types of measures include advertising, shop structure, and assortment policy.

Marketing activities are regulated by the law on marketing. The present law especially applies to incorrect or misleading marketing. Under this law it is also possible to intervene in marketing which does not provide reasonable or sufficient guidance.

Often this is not enough to ensure that essential information on foods reaches the consumer.

In the report NOU 1974: 61 on Advertising it is proposed that a law be introduced concerning mandatory information, to ensure better consumer information about goods and services. The report is now being studied by the Ministry of Consumer Affairs and Government Administration. The Government will take a stand on this proposal on the basis of the report and comments received.

One reason for the present situation may be a lack of knowledge at some levels in the chain of responsibility for the distribution and marketing of foods. This question is taken up in Section 8.8.

Measures in this area must be formulated in close cooperation with the individual sectors of the food trade. To a large extent it should be possible to base changes on agree-

ments with the different sectors, though if such agreements are to be respected by non-Norwegian interests it may be necessary to have the possibility of employing legal measures, including health regulations.

8.5 LARGE HOUSEHOLDS

There are considerable differences between the various groups of households. Individual measures which go beyond the general measures outlined in this chapter are felt desirable for the large households. These must especially include:

- education and further training for personnel in large households
- systematic cooperation between the large households in order to exchange and increase knowledge about the planning and operation of such households, and
- a direct and well-developed contact with the National Nutrition Council and other professional groups.

In the report on the education of personnel in large households (NOU 1975: 36) there is an attempt to clarify within the public sector:

- the need for leading kitchen personnel in hospitals and health institutions, boarding schools, military establishments, etc.,
- teaching plans for the various categories of such personnel,
- the need for instruction facilities, and measures to stimulate recruitment.

The report was presented in May, 1975, and the Ministry of Church and Education has sent it to interested authorities and organizations for comments. The Ministry of Church and Education on the basis of the report and the comments received will proceed with the matter further.

The large households constitute a very large wholesale purchaser of industrially produced foods and of kitchen equipment. An effective cooperation between these households could have a great influence on the development of the products offered, for the type of equipment to be used and for a number of other circumstances. The contact between the various households and groups of households can be improved. In a report which the Norwegian Productivity Institute has produced on completely and partially manufactured products for large households, it is proposed to establish a separate body to consider these questions.

Since many of the large households are publically owned and operated, the Government will contribute to establishing cooperation and seeing that this is extensive enough. However, a number of organizational questions remain which require clarification.

The running of large households must be based on professional knowledge acquired about nutrition. Efforts to increase the professional standards can be made in cooperation with the National Nutrition Council. The most important cooperation must be related to the professional content of the instruction given.

A more suitable diet in large households could contribute to a somewhat improved health situation generally and a more correct use of resources.

8.6 LEGISLATION

Current regulations in this area are aimed at:

- preventing the manufacture and sale of foods dangerous to health,
- ensuring cleanliness and hygienic conditions,
- stipulating how products shall be manufactured, their contents, and the requirements they must satisfy before they can be offered for sale,
- preventing incorrect conceptions as to the origin, condition, nature, quantity, or composition of products, or other circumstances which are of importance to public health, or for the consumer's assessment of the quality of the commodity.

The Government believes that laws and regulations can be useful and important means for carrying out the objectives of the nutrition and food policy.

Today a number of ministries administer various regulations which may be of significance for nutrition and food policy. The interministerial body, which this report proposes be established, will be given the task of seeing that the best possible coordination takes place in this area, and also of assessing the necessity for improving and simplifying the regulations.

A closer examination of current regulations concerning the declaration of the fatty acid content in foods, especially margarine, would be appropriate. It might also be of interest to develop new regulations for new products.

In this connection the Ministry of Social Affairs has appointed a committee to develop regulations for foods based on protein concentrates. An evaluation will also be made of whether there should be further requirements for declaring the nutrient content of various foods. Food inspection services play a central role in seeing that the regulations in this area are adhered to. This applies to quality control as well as hygiene control.

The hygienic tasks, for which the food inspection services are responsible, include the

control of microbiological pollutants and residues in food of pesticides and other biocides, heavy metals such as mercury, cadmium, etc., as well as additives, antibiotics, hormones, etc.

8.7 RESEARCH AND STUDIES

The implementation of the objectives proposed for food and nutrition in this report is dependent on the research input. As stated in Chapter 2—6 in this report, the research which is important for nutrition and food conditions covers a wide area. In the separate chapters it is noted that research requirements in the various fields are considerable.

It is outside the framework of this report to discuss research which is of importance for nutrition and food conditions generally. These questions are discussed to some extent in the Report No. 35 (1975—76) to the Storting on the organization and financing of research. The discussion in this report will be limited to research which has a more direct influence on the implementation of the nutrition and food policy measures discussed in Chapter 8.

There is in several areas today a limited knowledge of the most expedient way of carrying out nutrition and food policy measures. The implementation of the measures is a long-term process, and it is in several such areas pointed out that there is a need for research input.

There are a number of circumstances of importance to the implementation of the nutrition and food policy. These involve a number of different professional disciplines in research. The follow-up of the measures is shared between several different ministries, and in Chapter 9 it is proposed that this be coordinated by an interministerial body.

The Government feels there is a need for coordinating the research input which is necessary to strengthen measures to implement the nutrition and food policy. It is also necessary to make a priority and intersectorial evaluation of the projects undertaken.

It is not appropriate to discuss in this report the research areas which are of special importance. It is noted, however, that there is a need for research input aimed at changing the composition of raw materials, in connection with industrial processing, on factors which influence the diet of the population, and on special nutritional problems in our country.

In Report No. 35 (1975—76) to the Storting on the organization and financing on research, the Government has proposed that a body be established for research related to social planning. This body would look after

research tasks of an intersectorial and long-term nature within the administrative areas of the ministries.

The Government considers it natural that the proposed new body for research on social planning should also assume the responsibility for research activity related to the implementation of the future nutrition and food policy. There is relevant research work going on today under several institutes and research councils. Therefore, it would be a considerable task to coordinate this activity and develop good cooperation with other research councils and the various research institutes.

8.8 EDUCATION AND INFORMATION

8.8.1 Principle Assessment of Educational and Informational Activity

The purpose of this report is to plan a coordinated policy based on developing a nutritionally safe diet, while at the same time providing the basis for an increase in self-sufficiency through increasing production and changing consumption.

In the opinion of the Government, it is important that these perspectives are included in the educational and informational activity on these questions. The role of the schools is of special interest, because the implementation of the nutrition and food policy will be of a long-term nature.

Social development is characterized by a steadily greater division of labour between various occupations, while at the same time schools and the school situation differ essentially from the occupational situation. Fewer and fewer people know the process which is undergone, for example, from when grass is produced until milk stands on the table. There is less knowledge of nutritional content and the practical utilization and storage of raw materials today because the extent of processed foods has increased. The Government believes it is an important task for the schools to give the pupils both practical and theoretical insight into the production processes, and to reduce the division between production life and the educational situation. The activity in school gardens has contributed to practical knowledge about cultivating various fruits, berries and vegetables. It is thought natural that in the future this work be considered in connection with nutritional questions and the preparation of food. There are separate, typically seasonal peaks in both agriculture and fishing which require extra labour inputs, e.g. potato harvesting, sheep gathering, etc. It is felt natural that this be taken into consideration in school activities, so that the pupils participate in practical work, both as a part

of the teaching and as a step in carrying out production.

Cooperation has been established between the Ministry of Church and Education, the Norwegian School Garden Association and representatives of Hedmark and Oppland counties to develop models for school contact with agriculture. Public funds are used to subsidize experimental work in the counties, and it is planned that other counties will be offered the models which are developed.

There is also a corresponding question in principle within adult education and information; namely how the individual can adjust his own life pattern on the basis of nutritional considerations. In addition to knowledge of the basic principles there will probably be a need for instruction in food preparation and composition of a diet, having in mind a reduced fat intake. The practical cultivation of fruits, vegetables and berries could also create a greater interest in a practical implementation of the nutrition and food policy guidelines. The Government regards adult education, the encouragement of food growing in small gardens, allotment cultivation, etc. as important steps in implementing the nutrition and food policy.

8.8.2 Nutrition Instruction in Schools

The basis of our dietary habits is established at a very early age. It is therefore of great importance that teaching on nutrition questions occurs while children are small, and that this teaching is gradually followed up as the children become older. It should be noted that there are some unsolved tasks which must be further worked out in order to ensure the best possible instruction on matters of nutrition.

It is felt necessary that instruction in nutrition be given to nursery school teachers and other nursery school personnel. Instruction on nutrition should have a more central place in the three year nursery school teacher training.

In the case of the elementary school, teacher training must be strengthened — not only in regard to the study of home economics, but there must be efforts to make topics which include nutrition and the subject of diet a permanent part of the natural science sector and parts of the social sciences. No instruction on nutrition and diet is given in general teacher training. Another important task is to see that the textbooks maintain a satisfactory professional level. This can be achieved to a considerable extent by the use of nutrition consultants.

In order to improve instruction on nutrition in the short run, funds for teachers, courses, as well as teachers' manuals should be made available. This will be necessary to cover the needs of the elementary schools, especially in the lower grades, if the intentions of the Educational Guidelines as regards teaching of nutrition are to be fulfilled. Permanent solutions must be incorporated into the three year general teachers' training course.

In high school teaching — and especially for vocational training schools (schools for home economics and for the training of leading kitchen staff) it is a primary necessity to keep the teaching up to date. Therefore, opportunities for further training for teachers in such schools must be made available. In this connection the access which teachers have to institutions of higher education must be clarified, including questions of academic competence. Measures which provide teachers with the necessary economic opportunities to improve their teaching competence in nutrition will be of interest. Educational opportunities must also be adapted to the rules for the different levels of competence in teaching training.

The Council for Higher Education and the Council for Teachers Training will discuss the question of acquiring the suitable expertise to conduct courses in further and higher education.

The need for further education and additional courses also applies to groups employed in the processing and preparation of food, so that they can perform their jobs better. It should be mentioned that the mandate of the committee on the training of personnel in large kitchens primarily applies to the public sector. The private large household sector is not examined in the same way.

Experience and practical skills in individual households have a great influence on the diet. In the elementary school (the lower school and junior high school) emphasis is placed on the children being able to carry out practical activities parallel with the theoretical teaching. It is very important that this aspect of teaching is also strengthened in the future.

As regards high schools, the instruction in schools for home economics and the home economics courses given at vocational schools for trade and industry are of especially great importance.

Training is given to a total of 4,500 pupils per year at these schools. Both the practical and theoretical training will have a considerable influence on the development of the diet in individual households. This training should

be planned so that the objectives of the nutrition and food policy can be followed up in the individual households.

As mentioned previously the teaching material situation is not satisfactory. This also applies to circumstances which affect the whole teaching material situation, and which are being examined at present by a publicly appointed committee on teaching materials. Nevertheless, in the course of a short time it is necessary to find suitable solutions in the area of nutrition, both in regard to finding authors, coordinating practical and theoretical competence in the field, as well as arranging the necessary economic backing for the development of teaching materials. So far the Ministry of Church and Education has only supported the production of textbooks for use in vocational training. An extension of this support is now being assessed.

8.8.3 Special Remarks Concerning the Training of Health Personnel

Instruction on nutrition and diet is part of the training for different types of health personnel. This applies to nurses as well as doctors and dentists. The subject comes under physiology, where a study is made of body requirements for the different nutrients, including vitamins and minerals, and how these needs can be met through supplies of commonly available foods. In the study of diseases, the composition of the diet and different forms of dietary treatment for certain diseases are studied. Instruction is also given under the subjects of epidemiology and hygiene on the importance of diet in preventing deficiency diseases and ensuring good health.

Keeping in mind that all types of health personnel have the important task of including health information as part of their activities, and that information on correct diet plays an important role here, instruction on nutrition and diet should be given a better place in the curricula in the future. An assessment should be made to coordinate the somewhat diffuse opportunities for instruction which now exist, so that a comprehensive presentation of the subject is given in line with that which is usual for other disciplines.

It would also be important if diet and nutrition could be given a better place in higher and further education for medical personnel of all types.

8.9 INFORMATIONAL ACTIVITY

The purpose of informational activity is threefold:

- to motivate a more correct diet,

- to ensure a broad knowledge of the basic factors in this diet, and
- to provide an opportunity to acquire the necessary skills.

The objectives of this report are general in nature and are primarily defined in the form of national consumption and production goals. The requirements of an adequate and safe diet are the same for the majority of consumers, while the suitability requirement provides a broad framework within which each person and household can formulate their own dietary patterns.

The Government believes decisive emphasis must be placed on an effective information system to disperse the necessary knowledge and the corresponding skills.

An important condition for ensuring that informational activity is effective and adequately coordinated, is that an increased and improved informational activity is itself coordinated with the preparation of efficient and good teaching materials.

The activities of public bodies and organizations will often provide an important basis for informational work.

A coordinated information activity will also require planning for longer periods of time. In Chapter 9 it is proposed that planning and implementation come under the interministerial coordinating body for the nutrition and food policy.

The National Nutrition Council must be accorded the responsibility for seeing that the information activity which is carried out is balanced and within a reasonable professional framework.

The activities of the Consumer Council will be central in communication to the general public. A nationwide local activity has already been developed, which should be able to handle extended tasks in the years ahead.

In order to strengthen contacts with groups which work on nutrition questions, the Government will take the initiative for holding conferences on nutrition at regular intervals. The purpose of these conferences will be to ensure a broad discussion of important and current nutrition questions, to secure good contacts with and between the various sectors, and to spread information.

The National Association for Nutrition and Health holds a special position among the private organizations. The association should continue its work in guidance and providing advice and information on nutrition and diet.

The informational activities should take advantage of the wide and objective interest which already exists on nutrition questions in the humanitarian and other voluntary or-

ganizations and among the information organizations in the country. The Government believes that a considerable part of the information work should be carried out by such organizations and suitable information material should be made available for this. The Government feels public subsidies should be given for such activity and proposes that one million N. kr. be made available for this purpose.

This information work should be useful to all groups in the population, but nevertheless special attention should be given to some groups:

- health personnel
- children, who do not yet have established dietary patterns
- elderly
- risk groups, consumers who are especially susceptible to illness because of diet
- employees in large households.

Even if a person has sufficient motivation

and knowledge to reorganize his diet in a more correct direction, the necessary skills are vital.

There is a great need for suitable study material for adult education.

It is assumed that course activity in the field of nutrition will be undertaken in close cooperation with and between the information organizations in the country.

The need for teaching aids in this subject field is not limited to adult education. Those involved in education and other guidance work need periodicals, books and other professional literature for their own information. Educational and guidance work requires a varied and wide choice of aids: films, slides, flannel pictures and other visual instruction aids, textbooks and reference books, brochures, etc. Journalists who write on nutritional questions in newspapers, magazines, etc. should also have access to professional material of proper quality.

Chapter 9. Institutions for the Follow-up of the Nutrition and Food Policy

A number of public and private institutions and organizations have been interested in and have worked on nutrition questions. The implementation of the nutrition and food policy will depend on this work continuing and being stimulated in the future. There is a more detailed examination of the tasks in the educational sector in Chapter 8. Private and voluntary efforts should be carried out in accordance with the objectives drawn up in this report, and can be stimulated in various ways by public measures.

This chapter will examine in more detail the public institutions and their tasks in regard to the nutrition and food policy, i.e. that which was discussed in Chapter 8. Follow-up tasks and responsibilities related to the supply policy will not be discussed here.

Nutrition matters are the responsibility of the Directorate of Health in the Ministry of Social Affairs. The National Nutrition Council is its main advisory body.

9.1 NATIONAL NUTRITION COUNCIL

Following the establishment of Food and Agriculture Organization of the United Nations (FAO) the National Nutrition Council was established by Royal Decree of August 30, 1946.

According to its present terms of reference, the National Nutrition Council shall be an advisory body for Government administration and other public authorities in matters concerning nutrition.

The Council shall further cooperation between the institutions and organizations which are involved with tasks which have an influence on and are of importance for nutrition. It shall itself undertake nutritional studies with the funds placed at its disposal under the national budget, as well as other available funds. It shall further attempt to coordinate present and future scientific and practical work in the fields of nutrition research and food production.

The Council in cooperation with the ministries and other bodies concerned prepares reports requested by FAO, sees that the reports are sent at the right time, and also maintains other contacts with FAO.

The importance of the Council has lain largely in its function as a contact and coordinating body within the field of nutrition.

The members of the Council, at present 18 in number, are appointed by the Ministry of Social Affairs, and comprise research workers and other professional persons connected with nutrition and food research, as well as

representatives of the authorities and trade organizations concerned.

At present the Nutrition Council has the following subsidiary committees:

The Committee on Nutrition is responsible for the professional nutritional aspects of the Nutrition Council's activities and has served as the expert body for the Directorate of Health and other authorities.

The Committee on Food Supply prepares annual reports on the size and composition of domestic food production, market coverage and consumption of foods, as well as the relative consumption of domestic and imported foods.

The FAO Committee is responsible for the international aspects of the work of the Nutrition Council.

In addition, a committee to elaborate and up-date food composition tables and a committee on matters related to flour and bread have been established.

The National Nutrition Council received its terms of reference by Royal Decree of July 29, 1956. Directives to the Committee on Nutrition were laid down by the Directorate of Health in a letter of December 17, 1962 (see Appendix 7, not translated).

At present, the secretariate of the National Nutrition Council has two fulltime posts and shares office premises with the secretariate of the National Codex Alimentarius Committee.

9.2 FOLLOW-UP OF THE NUTRITION AND FOOD POLICY

In this Report to the Storting the Government has outlined a Norwegian nutrition and food policy.

The next phase will be to implement the policy through practical measures. It is evident from other parts of the report that nutritional questions influence a number of other areas in society. It is obvious that the implementation of the nutrition and food policy will require a continual balancing of nutritional considerations in relation to other considerations. The areas of responsibility of a number of ministries will be affected by this policy. It can not be expected that the nutrition and food policy objectives in this report can be reached quickly. It will require a period of at least 10 to 15 years, with an adaptation of activity in various areas.

If the nutrition and food policy objectives are to be reached, it will be vital to establish close cooperation with trade organizations, firms, various household groups, voluntary organizations and research institutions

On this background, the authorities must establish institutions which will ensure the coordination and future continuation of the nutrition and food policy.

Various administrative solutions are possible. The following is a list of a number of important tasks for which public bodies must be responsible:

- to describe and analyse both short- and long-term developments in diet and nutrition in relation to the nutrition and food policy objectives,
- to define projects and develop plans for both the long-term and annual implementation of the nutrition and food policy,
- to propose measures,
- to ensure that the necessary measures are carried out within specific time limits,
- to coordinate the work carried out by the different ministries and ensure that nutrition and food considerations are given sufficient emphasis in the various areas,
- to assess the effectiveness of the work which is carried out,
- to contribute to a satisfactory professional development in the field of nutrition,
- to ensure cooperation with trade and voluntary organizations,
- to give advice to governmental and other public authorities.

The implementation of a nutrition and food policy must be based on a long-term rearrangement of measures which have already been introduced. The responsibilities for these measures is mainly divided between:

The Ministry of Fisheries (fisher policy, domestic sales of fish and fish products)

The Ministry of Consumer Affairs and Government Administration (family, consumer and price questions)

The Ministry of Trade and Commerce (retailing, import regulations)

The Ministry of Church and Education (basic education, adult education, content in teaching and textbooks in a number of types of schools)

The Ministry of Environment (management of resources)

The Ministry of Agriculture (agricultural policy, import regulations)

The Ministry of Social Affairs (health questions, food inspection)

The Ministry of Foreign Affairs (international aspects of the nutrition policy)

The areas of responsibility of the different ministries are mentioned briefly in order to give an impression of the varied and extensive spheres which are affected by nutrition and food policy. In addition, a number of ministries will have tasks in connection with

the supply policy for the country. As mentioned previously, the latter aspect will not be discussed in this chapter.

In order to ensure that the different measures introduced by the authorities are in accordance with the nutrition and food objectives, there will have to be an effective co-ordination of activity in areas which influence the diet. Coordination also implies that the individual ministries must be familiar with the work which takes place in other ministries.

Decisions on the introduction of measures in this field will often have political implications. These will have to be considered by the political authorities.

The implementation of a national nutrition and food policy, especially in the first period, will have to be based on the fact that relatively strong political direction and coordination of the work may be necessary.

Measures in this area must have as sound a professional foundation as possible. The viewpoints in this report are based on the knowledge which exists today on nutrition, health and diet. Further knowledge on these questions may lead to a differentiation of the objectives outlined in Chapter 7. A sufficiently competent and broad professional environment is necessary.

Within the sphere of nutrition, it must also be expected that general development and new research inputs will necessitate changing content, goals and measures. It is therefore important that the practical implementing of nutrition and food policy is conducted according to such developments.

In order to ensure satisfactory coordination of planning and implementation of nutrition policy, and in order to ensure that it has a sound professional foundation, the Government will advocate the following administrative solutions:

1. Establishment of an interministerial co-ordinating body.
2. Reorganization of the National Nutrition Council.
3. Establishment of an office for nutrition in the Ministry of Social Affairs.

9.2.1 Coordinating Body for the Ministries

As mentioned earlier, there are several ministries responsible for areas which influence nutrition and diet.

The individual ministries must be made responsible for ensuring that the nutrition and food policy is taken into consideration in the professional areas with which they are concerned.

As the Government wishes to plan a more

defined nutrition and food policy, however, there will be a need for reciprocal information and a coordination of efforts in the different ministries.

In order to ensure that nutrition and food policy considerations are taken, the Government feels it necessary to establish a body to coordinate work on this policy in the ministries. This body shall not have coordinating responsibility for the food supply policy.

It shall define projects and prepare plans for both the long-term and annual implementation of nutrition and food policy.

Further, it shall ensure that the necessary measures are carried out within accepted time frameworks. Members of the Government will be kept informed of current work through the coordinating body. Parliament should preferably be oriented by means of the annual budget proposals from the ministry which is responsible for coordinating the nutrition and food policy and from the other individual ministries concerned.

The ministries shall be represented on the coordinating body by one or more civil servants working in the areas concerned.

9.2.2 Future Tasks and Membership of the National Nutrition Council

The Government will advocate a certain alteration of the terms of reference and membership of the National Nutrition Council. The present terms of reference of the Nutrition Council are given in Appendix 7 (not translated).

The Government will continue to have need for a body which can give professional advice on nutrition and food questions. In many matters concerning nutrition and diet, an all-round competence is required which no single person or professional group possesses.

The nutrition and food policy involves nutritional, physiological and hygienic, as well as economic, technical and consumer policy matters. Professional advice to the Government should contain evaluations on all these aspects.

On this basis, the following tasks can be outlined for the National Nutrition Council:

1. Be an advisory body for Government administration and other public authorities on matters concerning nutrition.
2. Give professional advice and assessments to others, e.g. voluntary organizations, large households, the food industry.
3. Be responsible for defining and analysing the diet situation in Norway in the short and long term.
4. Propose measures.
5. On the basis of a professional evaluation,

make recommendations on the distribution of funds for informational activity.

6. Contribute to a satisfactory professional development in the field of nutrition.
7. Assess the effectiveness of nutrition activities in Norway.

The Nutrition Council should consist of professional persons working within the various fields involving nutrition, consumer and supply questions.

Because the tasks of the Council will involve making professional evaluations for use in the ministries, the individual ministries should not be directly represented on the Nutrition Council.

The Nutrition Council has a number of subcommittees. The need for and composition of these should be evaluated by the new Nutrition Council. However, mention can be made here of the importance of making and maintaining contact with the research environments connected with nutrition, diet, food supply and the composition of foodstuffs.

The Nutrition Council should be given the economic means to commission professional studies by other institutions as a step to encourage professional development in the field of nutrition.

It is assumed that in the future the Nutrition Council will be primarily engaged in dealing with national nutrition and food supply matters, and that international matters which have so far been handled by the secretariat of the National Nutrition Council could be handled by the ministries concerned, i.e. primarily the Ministry of Agriculture, the Ministry of Fisheries and the Ministry of Foreign Affairs.

The Nutrition Council should as now be administratively associated with the Ministry of Social Affairs.

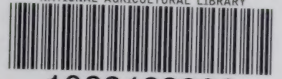
9.3 ADMINISTRATIVE FOLLOW-UP

On the basis of a total evaluation, the Government has decided that the administrative responsibility for the nutrition and food policy should continue to lie with the Ministry of Social Affairs.

Because of the increased emphasis placed by the Government on the nutrition and food policy, as expressed in the proposal for an interministerial coordinating body, a separate office for nutrition questions should be established in the Ministry of Social Affairs.

The office will be given the responsibility for the administration of nutrition matters. This implies that the office must, inter alia, assume the secretariat functions for the interministerial coordinating body and for the National Nutritional Council and its subcommittees.

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